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EFFECTS OF INTERMITTENT ALTITUDE EXPOSURES ON ACCLIMATIZATION TO 4,300 M

U.S. ARMY RESEARCH INSTITUTE
OF
ENVIRONMENTAL MEDICINE

Natick, Massachusetts
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This study examined the effects of 3 wk of intermittent exposures (4 h/d, 5 d/wk) to 4,300 m altitude-equivalent, in combination with either passive sitting or exercise training, on the process of altitude acclimatization. Physiological, hematological, physical work performance, and acute mountain sickness (AMS) responses elicited by intermittent exposures to altitude were compared to previously published data from chronic altitude residence. Six adult lowlanders (30±2 yrs; 70±3 kg) were acutely exposed (i.e., 30 h) to 4,300 m altitude-equivalent once before (PreAc) and once after (PostAc) a 3-wk period of intermittent altitude exposures. Exercise training during intermittent exposures to altitude did not enhance the magnitude of altitude acclimatization. Thus, data from both groups were combined. Three weeks of intermittent altitude exposures resulted in an 11% increase in resting ventilation, 18% increase in maximal oxygen uptake (VO2max), 21% improvement in whole-body submaximal endurance performance, 26% increase in small-muscle endurance performance, and elimination of AMS symptoms from PreAc to PostAc. Intermittent altitude exposures accomplished 50%-100% of the expected adaptation to altitude, based on improvements in submaximal endurance performance and absence of altitude illness, when compared to previous chronic altitude residence studies. These large improvements in physical work performance and AMS symptomatology appear to be related to the large degree of ventilatory acclimatization achieved after 3 wk of intermittent altitude exposures. Our findings suggest that 3 wk of intermittent altitude exposures is a useful tool for enhancing physical work performance and eliminating symptoms of AMS in less total exposure hours than chronic altitude residence.

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USARIEM TECHNICAL REPORT T-????

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BACKGROUND

Mountain ranges typically form the borders of nations and are likely settings for various types of military operations involving military personnel. Numerous regions of geopolitical interest to the U.S. such as the Balkans, South America, the Middle East, and Asia contain extensive areas of moderate (>1500 m) to high (>2400 m) altitudes. Consequently, military personnel may be deployed to high mountain regions where they will need to acclimatize effectively to support their unit's mission. Altitude-induced illness and decrements in physical work performance, due to hypobaric hypoxia, can have a significant negative impact on attainment of mission objectives by military units rapidly deployed to high mountain terrain.

Current guidance provides commanders with two choices, staging and acetazolamide, to reduce the adverse effects of deployment to high mountain regions. Slowing the overall ascent rate by staging at intermediate elevations for periods of 1-7 days allows military personnel time to progressively acclimatize to altitude, thus minimizing altitude-induced illness and decrements in physical work performance. However, staging requires a substantial amount of time, deployment, and support of troops to progressively higher elevations. Thus, staging may not be a viable option or cost-effective strategy when rapid deployment is operationally essential. In conjunction with staging, or as its own intervention, acetazolamide provides prophylaxis against acute mountain sickness (AMS) and facilitates altitude acclimatization. However, acetazolamide may actually degrade physical performance due to the metabolic acidosis that it produces. Acetazolamide also has a high incidence of side effects that decrease its acceptability as a deployment strategy. The goal of this protocol was to evaluate a third option for inducing altitude acclimatization: intermittent altitude exposures. The theory behind this approach is that altitude acclimatization can be induced in low-altitude dwelling personnel by a regular schedule of short exposures to altitude, and that the addition of exercise during these short exposures to altitude will enhance the magnitude of the altitude acclimatization process. Validating this approach to altitude acclimatization should lead to feasible methods for providing intermittent altitude exposures to troops prior to deployment to high mountain regions.

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EXECUTIVE SUMMARY

Physical work performance is degraded in military personnel deployed to high mountain environments due to the lower partial pressure of oxygen in the ambient air (hypobaric hypoxia). Symptoms of acute mountain sickness (AMS), which include headache, anorexia, nausea, vomiting, insomnia, and lassitude, are likely to occur when military personnel are first deployed to high altitude. Physical work performance and symptoms of AMS are improved over time while living at altitude, as the body adapts to the lower partial pressure of oxygen. This process is called "acclimatization." Evidence from previous studies has shown that passive intermittent exposures to hypobaric hypoxia may also acclimatize an individual to altitude. Given that many of the physiological changes that occur with altitude acclimatization also occur with exercise training, the addition of exercise training during intermittent exposures to hypobaric hypoxia may provide a synergistic effect that enhances the acclimatization process. Therefore, the purpose of this study was to examine the effects of 3 wk of intermittent exposures (4 $h \cdot d^{-1}$, 5 $d \cdot wk^{-1}$) to 4,300 m altitude-equivalent, in combination with either passive sitting or exercise training, on the process of altitude acclimatization. Physiological, hematological, physical work performance, and acute mountain sickness (AMS) responses elicited by intermittent exposures to altitude were compared to previously published data from chronic altitude residence. Six adult lowlanders (30±2 yrs; 70±3 kg) were acutely exposed (i.e., 30 h) to 4,300 m altitude-equivalent once before (PreAc) and once after (PostAc) the 3-wk period of intermittent altitude exposures. Exercise training during intermittent exposures to altitude did not enhance the magnitude of altitude acclimatization. Thus, data from both groups were combined. Three weeks of intermittent altitude exposures resulted in an 11% increase in resting ventilation, 18% increase in maximal oxygen uptake (VO_{2max}), 21% improvement in whole-body submaximal endurance performance, 26% increase in small-muscle endurance performance, and elimination of AMS symptoms from PreAc to PostAc. Intermittent altitude exposures accomplished 50%-100% of the expected adaptation to altitude, based on improvements in submaximal endurance performance and absence of altitude illness, when compared to previous chronic altitude residence studies. These large improvements in physical work performance and AMS symptomatology appear to be related to the large degree of ventilatory acclimatization achieved after 3 wk of intermittent altitude exposures. Our findings suggest that 3 wk of intermittent altitude exposures is a useful tool for enhancing physical work performance and eliminating symptoms of AMS in less total exposure hours than chronic altitude residence.

INTRODUCTION

Acclimatization to high terrestrial altitude is the result of a series of integrated changes in physiology that function to compensate for the lower partial pressure of oxygen in the ambient air (P_IO_2). The magnitude and time sequence of these physiological changes are determined by the degree of hypoxic stress generated by the rapidity and magnitude of ascent. Successful acclimatization usually occurs after a 2-3 wk residence at altitude, and is most readily apparent as an increase in submaximal endurance performance and absence of altitude illness (116).

Physiological variables that contribute to the increase in submaximal endurance capacity with altitude acclimatization include an increase in exercise minute ventilation ($\dot{V}E$) (21,77) and decrease in plasma volume (PV) (39,96,101,113). These changes cause respective increases in arterial oxygen saturation (SaO_2) and hemoglobin concentration ([Hb]). The increase in [Hb] occurs primarily due to a decrease in PV since red blood cell mass and erythropoietin concentration ([EPO]) are not increased after a 2-3 wk altitude acclimatization period (61,96). Since arterial oxygen content (CaO_2) is determined by both SaO_2 and [Hb], CaO_2 is reduced upon initial ascent to altitude, due to the lower partial pressure of arterial oxygen (PaO_2), and increased with altitude acclimatization (35). This increase in CaO_2 with acclimatization alleviates the demand for an increased blood flow to supply oxygen requirements to the body. Thus, after acclimatization there is a reduction in maximal cardiac output, likely due to the decrease in stroke volume and heart rate (HR), which offsets the increase in CaO_2 and, therefore maximal oxygen uptake ($\dot{V}O_{2max}$) remains unchanged. However, the reduction in circulatory strain at a given submaximal workload likely contributes to the increase in submaximal endurance performance following altitude acclimatization (44,60). With altitude acclimatization, not only is whole-body submaximal endurance performance improved, small muscle endurance performance is also improved (27,28). Reasons for this may be related to improvements in muscle buffering capacity after altitude acclimatization (66,90), and/or a more limited increase in intramuscular $[H^+]$ due to less lactate accumulation ([La]) after altitude acclimatization (10,13,114).

Physiological variables that contribute to the decrease in AMS with altitude acclimatization include a lessening of the hypoxic stimulus and resolution of an altered fluid and electrolyte homeostasis (38,45,99,109). The hypoxic stimulus is lessened by an increase in resting $\dot{V}E$ with altitude acclimatization that causes an increase in PaO_2.

Since AMS is widely speculated to be the result of an increase in extracellular fluid volume and resultant cerebral edema, caused initially by the hypoxic stimulus, the resolution of AMS involves a moderate diuresis to decrease the extracellular fluid retention. In fact, one study (99) found that soldiers with AMS showed evidence of fluid retention, while soldiers free of symptoms had lost body weight and increased their urine output. With acclimatization to altitude, most studies show a significant decrease in PV and total body water (45,95), which serves to both increase CaO_2, by increasing [Hb], and decrease extracellular fluid volume and cerebral edema. Both of these factors probably contribute to the decrease in AMS with altitude acclimatization.

Thus, acclimatization to altitude allows the normal lowlander to successfully work and reside at altitude with little or no symptoms of AMS. However, living at altitude on a continuous basis is somewhat undesirable due to the possible negative effects of isolation, tight living quarters, immunosuppression (54), increased oxidative stress (98), sleep disturbances (46), and general malaise (109). Furthermore, this 2-3 wk acclimatization process is long for individuals who need to rapidly deploy and work, compete, or climb at altitude upon arrival. Thus, if acclimatization to altitude can be accomplished by intermittent exposures to altitude, soldiers could reduce their daily exposure time to altitude and avoid some of the negative drawbacks associated with living at altitude. In addition, if the intensity of the hypoxic stress is increased by performing exercise at altitude, the degree of altitude acclimatization achieved may be greater than that achieved with passive intermittent exposures to altitude. There are hints within the literature that both of these solutions may be possible.

Nagasaka and Satake (72) found in trained mountaineers that resting $\dot{V}E$ increased ~51% and resting HR decreased 18 beats•min^{-1} from the first to the third day of intermittent 6 h•d^{-1} resting exposures to 6000-8000 m. However, red blood cell count ([RBC]) was not changed. Savourey et al. (92,93) reported in trained mountaineers that resting and exercise $\dot{V}E$ were increased 19% and 37%, respectively, from the first to fifth day of 8 h•d^{-1} exposures to 4,500 -8,500 m. Resting and exercise SaO_2 were also increased 5% and 10%, respectively. Hematological and hormonal changes in this study were characterized by an 18% increase in [EPO], 44% increase in the percentage of reticulocytes, 150% increase in norepinephrine concentration ([NOR]) but no change in [Hb] and [RBC]. Casas et al. (19) reported significant increases in [Hb], hematocrit (Hct), and [RBC], and a right-shifted [La] versus workload curve after trained mountaineers performed low intensity exercise during intermittent exposures to 4000-

5,500 m for 3-5 $h \cdot d^{-1}$ for 17 d. These studies on trained mountaineers suggest that resting intermittent exposures to a high altitude (i.e., 4,500-8,500 m), in combination with no exercise or low intensity exercise, result in a large degree of acclimatization to a lower altitude (i.e., 4,300 m). However, none of these studies used control groups. Furthermore, no measurements of AMS or submaximal endurance performance, two key indices of successful altitude acclimatization, were made in these studies. Also, due to the fact that the subjects in these studies were trained mountaineers exposed to very high altitudes, there are limited inferences that can be made from these studies as to how the lowlander intermittently exposed to a moderate altitude will acclimatize.

Four studies involving no exercise have examined the lowlander intermittently exposed to "altitude" in which sleeping was not part of the intermittent altitude exposure. Burse and Forte (18) measured AMS in lowlanders after breathing a hypoxic gas mixture that simulated 3,200 -3,550 m for 8 $h \cdot d^{-1}$ for 10 d and compared their responses to a group of controls. They reported no differences in AMS after 48-h of exposure to 4,500 m in a hypobaric chamber between the hypoxic gas and control group. However, this study was complicated by the fact that the actual degree of hypoxemia (i.e., SaO_2) was never measured while subjects were breathing the hypoxic gas mixture. A recent study by Katayama et al. (51) reported no change in VO_{2max} and HR_{max}, measured in hypobaric hypoxia, after lowlanders were exposed to 4,500 m for 1 $h \cdot d^{-1}$ for 7 d, but found a 5% increase in resting and maximal exercise SaO_2. Rodriguez et al. (87) reported significant increases in resting SaO_2, [Hb], Hct, [RBC], and reticulocytes in lowlanders intermittently exposed to 4,000-5,500 m for 90 $min \cdot d^{-1}$ for 3 $d \cdot wk^{-1}$ for 3 wks. Ricart et al. (80) reported no change in resting [Hb] and Hct, a 6% increase in exercise SaO_2, and a 22% increase in exercise $\dot{V}E$, measured in hypobaric hypoxia, in lowlanders exposed to 5000 m for 2 $h \cdot d^{-1}$ for 14 d. All of these studies on lowlanders suggest that **resting** intermittent exposures to high altitude induce a large degree of ventilatory acclimatization and some degree of hematological acclimatization. However, as in the studies on trained mountaineers, adequate measures of AMS and submaximal endurance performance were not made.

Exercising at 65%-70% of VO_{2max} at 4,300 - 4,500 m induces a 5%-10% arterial desaturation compared to resting SaO_2 at those altitudes (7,11,49). This amount of desaturation is equivalent to sitting at an altitude of ~ 5,000-5,500 m (110). Thus, the addition of exercise at a given altitude is another way to provide a greater hypoxic stress to the body without increasing the exposure altitude. Thus, it may be

hypothesized that exercising during intermittent exposures to altitude should induce a greater degree of acclimatization than just passive sitting during intermittent altitude exposures. Several studies have been done that focused on whether exercise training in untrained volunteers during intermittent exposures to altitude provides any additional benefit in improving exercise performance (Table 1). A summary of the mean results from these studies indicates a mean ~10% increase in VO_{2max}. Engfred et al. (25) also reported a 256% improvement in submaximal endurance exercise performance. These large performance improvements were attributed primarily to ventilatory and muscle tissue adaptations that occurred with intermittent exposures to altitude. However, these studies did not include non-training control groups passively exposed to altitude in order to accurately determine the effects of hypoxia apart from the effects of exercise training. Furthermore, many of these studies measured their post-acclimatization effects at sea level rather than at altitude. Lastly, when endurance-trained volunteers were used as subjects in studies involving exercise training during intermittent exposures to altitude, none reported improvements in VO_{2max} (56,63,103,104) but one reported an increase in submaximal exercise performance (104). Thus, the training status of volunteers before beginning a program of intermittent altitude exposures may affect post-intermittent exposure exercise performance results.

Table 1. Results from Nine Studies Measuring Maximal Oxygen Uptake (VO_{2max}) in Untrained Volunteers Before and After a Period of Combined Exercise Training and Intermittent Exposures to Hypobaric Hypoxia or Hypoxic Gases.

Study	Altitude (m)	Training Intensity (% altitude VO_{2max})	Days	Days •wk^{-1}	Minutes •Day^{-1}	Total Hours	Pre-training VO_{2max} (l•min^{-1})	Post-training VO_{2max} (l•min^{-1})	% Change in VO_{2max}
(14)	4,500-5,700	~70-80	21	6	120	36	1.97	2.06	4.8
{1094, 1088}†	2,500	~70	35	5	45	19	3.05	3.42	12.1*
(24)†	2,500	~70	35	3	45	11	3.69	4.27	15.7*
(88)	3,450	~60	28	6	30	12	2.88	3.29	14.2*
(22)	4,100-5,700	~70-80	22	6	120	36	2.53	2.81	11.1*
(70)†	4,000-6,000	~70	21	2	40	4	2.86	3.08	7.7
(106)	3,850	~65	42	6	30	18	3.15	3.42	8.6*
(50)†	4,500	~70	14	5	30	5	3.67	3.94	7.1*
(62)†	2,500	~60-70	56	3-4	60	28	2.69	3.00	12.4*
Mean	**3,811**	**~70**	**30**	**5**	**58**	**18**	**2.94**	**3.25**	**10.5**

*Indicates significant change in VO_{2max} from pre- to post-training. †Indicates pre- and post-measurements were made at sea level.

The effects of exercise training while residing at altitude have already been extensively reviewed (29) and collectively, the results suggest that both improvements in VO_{2max} and submaximal endurance exercise performance, measured at high altitude, occur following a period of exercise training and residence at low, medium or high altitudes. This finding is in contrast to the reported lack of improvement in VO_{2max} following chronic altitude residence without exercise training. Thus, the improvements in exercise performance under these circumstances are most likely related to the well-known beneficial effects of exercise training rather than the adaptations that occur with altitude acclimatization. Similarly, the effects of exercise training while residing at altitude for a significant portion of the day (i.e., sleep high, train low) have been extensively reviewed (29,112) and although controversial (3-5) suggest that living high (i.e >16 h•d^{-1}), training low improves post-altitude sea level performance due to increases in red blood cell mass and maintenance of training intensity (58,100).

To our knowledge, only two studies have been done that compared passive sitting and exercise training during intermittent exposures to hypobaric hypoxia to determine whether exercise training is beneficial in the altitude acclimatization process. In one study, trained mountaineers exercised for 30-75 min d^{-1} at a HR < 120 beats min^{-1} at 5,500 m in a hypobaric chamber for 9 d, and their responses were compared to a group of controls resting at the same altitude (86). No difference in $\dot{V}O_{2max}$, measured at sea level, was reported between the two groups before and after the intermittent exposures. However, no measurements were made at altitude, and the amount of desaturation incurred in the exercise-training group was not reported. Although the exercise training intensity was likely too low in this study to elicit significant between-group differences, when results from both groups were combined, significant increases in [Hb], Hct, [RBC], and reticulocytes, and decreased [La] at submaximal workloads after intermittent altitude exposures were reported. Again, given that this study was done on trained mountaineers, the findings may not be applicable to the untrained lowlander intermittently exposed to altitude. In the other study (49), untrained lowlanders exercised at 65%-70% of their $\dot{V}O_{2max}$ at 4,500 m for 30 min d^{-1} for 6 d, and their responses were compared to a group of controls sitting at altitude. A 6% increase in $\dot{V}O_{2max}$, measured at sea level, was reported in the exercise training group while no increase in $\dot{V}O_{2max}$ was reported in the passive sitting group before and after intermittent altitude exposures. Again, in this study, no physiological or performance measurements were made at altitude, except for resting SaO_2, which was not different between the groups. Furthermore, this study made no physiological measurements during exercise at altitude, and exercise responses may differ markedly from resting responses.

In summary, previous studies suggest that intermittent altitude exposures, with or without exercise, will induce altitude acclimatization. However, no previous study has evaluated the effects of intermittent altitude exposure and exercise training on reducing the occurrence of AMS and improving submaximal endurance performance following a rapid ascent to altitude.

OBJECTIVES

The objective of this study was to examine the effect of intermittent altitude exposures, combined with either passive sitting or exercise training, on the process of altitude acclimatization. Altitude acclimatization was induced by 3 wk of intermittent

exposures (4 $h \cdot d^{-1}$; 5 $d \cdot wk^{-1}$) to 4,300 m altitude-equivalent in a hypobaric chamber, and results were compared to previously published data from chronic altitude residence studies. The following were assessed during an acute 30-h exposure to altitude both before and after a 3-wk period of intermittent exposures to hypobaric hypoxia: (1) specific ventilatory, cardiovascular, hematologic, body fluid, hormonal, and other physiological measurements indicative of early altitude acclimatization, (2) frequency and severity of signs and symptoms of AMS; (3) maximal oxygen uptake (VO_{2max}); (4) submaximal whole-body endurance performance (END_{wb}); and (5) small muscle endurance performance (END_{sm}). We hypothesized that both passive sitting and exercise training during intermittent exposures to 4,300 m altitude would partially acclimatize an individual to 4,300 m altitude. We further hypothesized that exercise training during intermittent exposures to 4,300 m altitude would have a greater effect on acclimatizing an individual to 4,300 m altitude.

METHODS

SUBJECTS

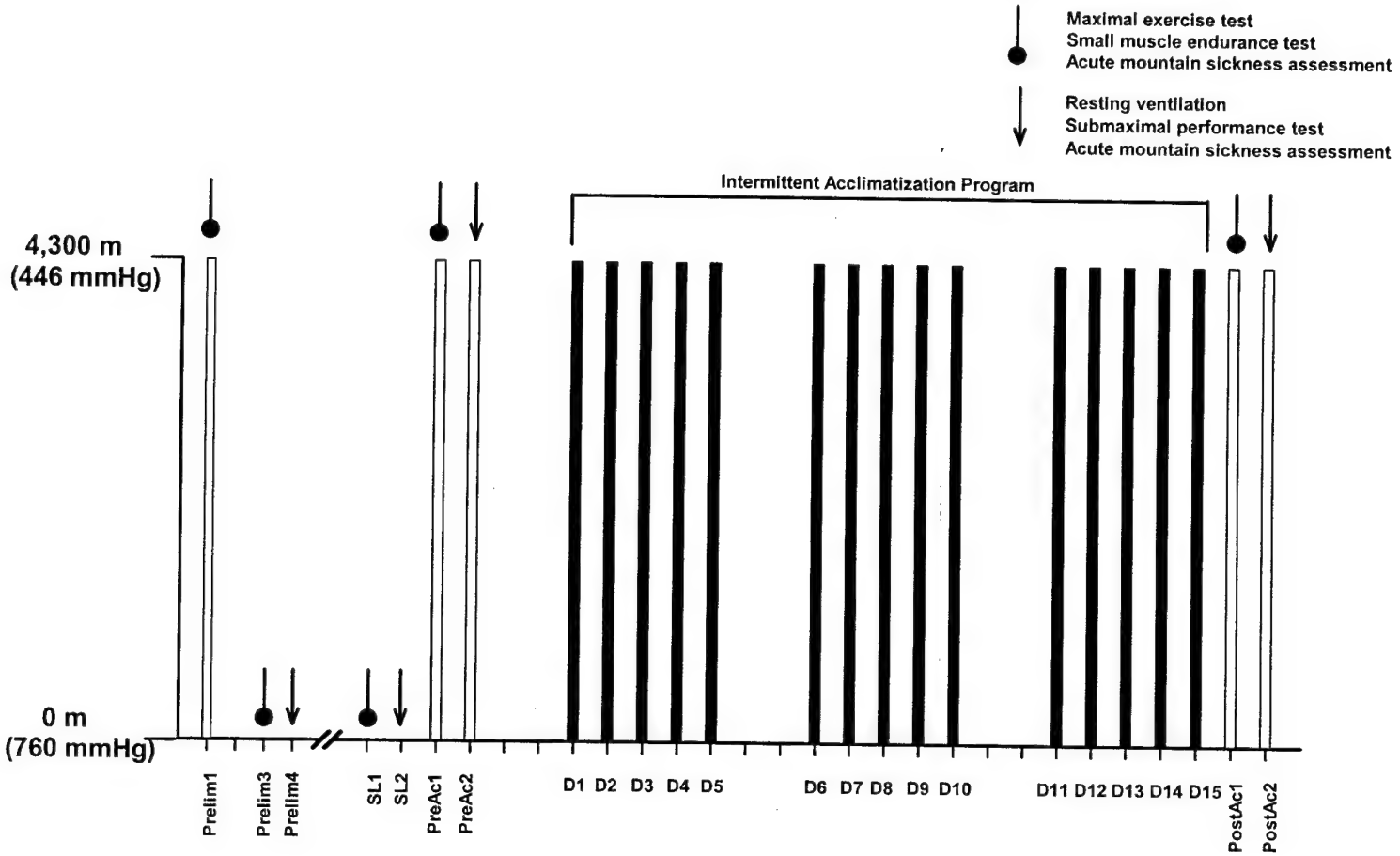
Six nonsmoking volunteers (5 male, 1 female) with a mean (±SD) age and body weight of 23±4 yrs and 66±10 kg, respectively, participated in this study. Each was a lifelong low- altitude resident and had no exposure to altitudes greater than 1,000 m for at least 6 months immediately preceding the study. All volunteers received medical examinations, and none were found to have any condition that would warrant exclusion from the study. All had normal [Hb] and serum ferritin levels. The female had a normal menstrual cycle length (28±2) over the 2-month testing period, had not taken oral contraceptives or hormone therapy for at least 6 months before entering the study, and had never been pregnant. All participated in regular sea-level physical training (2-3 $h \cdot wk^{-1}$) before and during the study and were of average physical fitness. Each gave written and verbal acknowledgment of their informed consent and was made aware of their right to withdraw without prejudice at any time. Investigators adhered to Army Regulation 70-25 and U.S. Army Research and Materiel Command Regulation 70-25 on the use of volunteers in research.

PROTOCOL

Design

This study used an unblinded two-factor (i.e., time and group) experimental design in which each test volunteer's specific ventilatory, cardiovascular, hematologic, body fluid, hormonal, and other physiological measurements indicative of early altitude acclimatization, frequency and severity of signs and symptoms of AMS, $\dot{V}O_{2max}$, END_{wb}, and END_{sm} were evaluated during preliminary measurements, at sea level (SL), and during $\leq$30 h exposures to 4,300 m altitude-equivalent (P_B=446 mmHg) before (PreAc) and immediately after (PostAc) a 3-wk intermittent (4 h•d^{-1}; 5 d•wk^{-1}) altitude (4,300 m) exposure protocol (Figure 1). Prior to SL testing, test volunteers were familiarized with the hypobaric chamber during a 6-h exposure to hypobaric hypoxia, during which they performed a $\dot{V}O_{2max}$ test, small muscle endurance performance test, and filled out AMS questionnaires, in order to reduce the novelty factor involved with performing exercise and reporting subjective symptoms of AMS at altitude. All volunteers also performed a preliminary $\dot{V}O_{2max}$, submaximal whole-body endurance performance test, resting ventilation test, and small muscle endurance performance test at SL to reduce the learning factor involved in performing these tests. On the first day of testing during the 30-h SL, PreAc, and PostAc exposures, $\dot{V}O_{2max}$, END_{sm}, and AMS symptomatology were measured. On the second day of testing, resting ventilation, END_{wb}, and AMS symptomatology were measured. Each exercise test was performed at approximately the same time of day and same number of hours after the last meal in each testing condition.

Figure 1. Time course of the experiment



Preliminary Phase (Prelim1, Prelim3, Prelim4); Sea Level (SL1, SL2), Pre-Acclimatization (PreAc1, PreAc2)
Intermittent Acclimatization Program (D1-D15), Post-Acclimatizaton (PostAc1, PostAc2)

Training Program

Three of the test volunteers were assigned to the passive sitting (PS) group, and three of the test volunteers were assigned to the exercise training (ET) group. One volunteer in the PS group (male) injured his thumb during the course of the study. Thus, his data were eliminated from further END_{sm} analysis.

Volunteers were weighed each morning of the training program (wearing t-shirts, shorts, and socks) and were encouraged to maintain their pre-study body weight throughout the study. The exercise-training program consisted of biking in the hypobaric chamber on a bicycle ergometer 5 $d \cdot wk^{-1}$ for 3 wk. The ET group warmed up at 60 W on a bicycle ergometer (Model 818E, Monark, Varberg, Sweden) for 15 min after arriving at an altitude equivalent of 4,300 m (446 mm Hg). After the 15-min warm-up, training began. During the first week, training was maintained at a constant exercise intensity for 45 $min \cdot d^{-1}$ at a HR corresponding to 70% of the pre-training altitude VO_{2max}. During the second week, 3 d of constant rate training lasting 45 $min \cdot d^{-1}$ at the same HR as the first week and 2 d of interval training at a HR corresponding to 85% and 40% of pre-training VO_{2max} (3 min on, 3 min off, respectively) lasting a total of 42 $min \cdot d^{-1}$ were completed. During the third week, 3 d of constant rate training lasting 1 $h \cdot d^{-1}$ at the same HR as the first week and 2 d of interval training similar to the second week were completed. Workloads were adjusted as necessary as the training program progressed to ensure achievement of appropriate training HR. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) using a sphygmomanometer (Baumanometer, W.A. Baum, Co, Copiague, NY) and the auscultatory method, arterial oxygen saturation (SaO_2) using finger pulse oximetry (Model N-200, Nellcor, Pleasanton, CA), and heart rate (HR) using wireless heart rate watches (Model 8799, Computer Instruments Co, Hempstead, NY) were periodically measured on both groups of volunteers every day during the training sessions

At the end of all the training sessions, all test volunteers remained resting in the hypobaric chamber so that their total exposure time to hypobaric hypoxia, including decompression, totaled 4 $h \cdot d^{-1}$. Both groups were allowed to watch videos, write letters, and listen to music following the training sessions. After the 4 $h \cdot d^{-1}$ altitude exposure, the chamber was recompressed over 15 min, and the test volunteers were released from testing for the day. They were encouraged to drink water to replace any fluid loss during exercise and/or altitude exposure. All volunteers were required to

maintain their 2-3 d•wk^{-1} SL training program to maintain their pre-study level of physical fitness. Physical activity monitor logs were kept throughout the 6-wk study.

Environmental Conditions

All testing was performed in a hypobaric chamber that was maintained at a temperature and relative humidity of 21±2°C and 45±5%, respectively. The SL testing was performed at ambient barometric pressure (~760 mm Hg), and the two "altitude" exposures were at an altitude-equivalent of 4,300 m (~446 mmHg). The training program was also conducted at an altitude equivalent of 4,300 m (~446 mmHg).

Diet

Volunteers were required to eat a pre-selected diet of commercially available frozen entrees, drinks, and snacks of known energy and nutritional content for the 30-h exposure. The quantity of food consumed was not limited but each volunteer recorded food intake. Twenty-four-hour urine volumes were also recorded during both days of testing at SL, PreAc, and PostAc. Volunteers were given identical meals for each 30-h exposure to limit the potential effects diet may have on both altitude-induced illness and exercise performance. Volunteers were not allowed to consume caffeine throughout the study. Volunteers were required to stop caffeine consumption 9 d before SL measurements to minimize any effect of caffeine withdrawal on altitude-induced illness scores.

MEASUREMENTS

Resting Ventilation

Resting ventilation measurements were performed in the morning after ~ 24-h exposure to altitude following a 12-h fast. The volunteers were resting in a seated position and breathed through a low resistance respiratory valve and breathing circuit connected to a computer-controlled, breath-by-breath open circuit metabolic measurement system (Vmax229, SensorMedics Co, Yorba Linda, CA). Resting ventilation tests measured the following: minute ventilation ($\dot{V}E$), oxygen uptake ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), and end tidal carbon dioxide ($PETCO_2$). The respiratory exchange ratio (RER) was calculated from $\dot{V}O_2$ and $\dot{V}CO_2$ measurements.

Resting SaO_2 was measured by pulse oximetry, and resting HR was measured by 3-lead electrocardiogram (ECG) (Model N-200, Nellcor, Pleasanton, CA). The resting ventilation tests were about 20 min in duration. Mean resting ventilation data were calculated from the last 8-10 min of the session.

Resting Hematologic Measures

Resting hematologic measures were made in conjunction with resting blood measurements taken prior to conduct of the maximal and submaximal exercise tests. They are described in detail under Blood Sampling and Analysis.

Altitude Illness Symptoms Assessment

Frequency and severity of AMS was determined from information gathered using the Environmental Symptoms Questionnaire (ESQ) and the Lake Louise AMS Scoring System (LLS). The ESQ is a self-reported, 68-question inventory designed to quantify symptoms induced by altitude and other stressful environments (91). To document the presence of AMS, a weighted average of cerebral symptoms (headache, lightheaded, dizzy, etc.) designated "AMS-C" and respiratory symptoms (short-of-breath, hurts-to-breathe, etc.) designated "AMS-R" were calculated from the ESQ. An AMS-C score greater than 0.7 and AMS-R score greater than 0.6 indicated the presence of AMS. The effectiveness of AMS-C scores in identifying individuals with AMS has been previously reported and validated (91). The LLS consists of a five- question self-reported assessment of AMS symptoms and a three-question objective assessment of clinical signs (82). It appears to successfully detect AMS and correlates with ESQ scores (8). The total LLS score, consisting of the sum of the self-assessment question score and the clinical-assessment score, and the self-report LLS score were calculated for each test volunteer. The ESQ and LLS were administered twice during the preliminary phase and four times (2 p.m., 8 p.m., 8 a.m., and 2 p.m.) in a 30-h period during the one SL and two "altitude" exposures. These time points corresponded to 6-h post, 12-h post, 24-h post, and 30-h post initial altitude exposure.

Exercise Performance Testing

Prior to all testing, the volunteers were required to abstain from alcohol for at least 24 h and not exercise on the testing day. The volunteers also maintained the

same diet for each of the 30-h exposures. Twenty-four hour dietary logs were analyzed for energy content and percent contribution of macronutrients (Nutritionist III v.6.0, Houston, TX).

Prior to each exercise test, the volunteer was weighed (wearing t-shirt, shorts, and socks) to the nearest 0.1 kg. During exercise, HR was determined from continuous ECG recordings (Cardiovit AT-6C; Schiller Canada, Inc., Nepean, Ontario), SBP and DBP were measured using an automated system (model 4240, Suntech, Raleigh, NC), and SaO_2 was measured by finger pulse oximetry. Respiratory gas measurements were made continuously during the $\dot{V}O_{2max}$ test and intermittently during the END_{wb} test using an open-circuit metabolic measurement system (Vmax 229, Sensormedics Co, Yorba Linda, CA) calibrated with certified gases and volume standard. The metabolic cart provided values for $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$. The RER was calculated from $\dot{V}O_2$ and $\dot{V}CO_2$ measurements. The ventilatory equivalent for O_2 ($\dot{V}E \cdot \dot{V}O_2^{-1}$) and CO_2 ($\dot{V}E \cdot \dot{V}CO_2^{-1}$) were calculated from individual $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$ data in order to minimize intra-subject variability in $\dot{V}E$ due to different body sizes and metabolic rates. The 20-point Borg rating of perceived exertion (RPE) was used to quantitate each volunteer's subjective assessment of overall physical effort during exercise testing (16). The O_2 pulse ($ml \cdot beat^{-1}$) was calculated as $\dot{V}O_2$ divided by HR. Mean arterial pressure (MAP) (mmHg) was calculated as 0.333 (SBP-DBP)+DBP.

Maximal Oxygen Uptake.

An incremental, progressive exercise bout to physical exhaustion on an electromagnetically braked bicycle ergometer (Model 800s, Sensormedics Co, Yorba Linda, CA) was used to assess each volunteer's $\dot{V}O_{2max}$ using a protocol similar to that described by Katch and Katch (52). Volunteers warmed up for 3 min at 60 W following resting measurements sitting on the bicycle ergometer. The workload was then increased to 80-100 W for females and 120-150 W for males for 2 min. Thereafter the workload was increased by 30 W at SL and 25 W at PreAc and PostAc every 2 min, until the volunteers were unable to maintain a constant pedaling rate of 60 rpm. The $\dot{V}O_2$ measured at exhaustion was considered $\dot{V}O_{2max}$ if two of the following criterion were satisfied: identification of a plateau in $\dot{V}O_2$ with an increase in power output (< 150 ml $\dot{V}O_2$ increase), post-exercise [La] > 8 mM, and respiratory exchange ratio > 1.15 (2). If two of the three criteria were not met, the volunteer, after a 5-10 min rest and 5-min warm-up, repeated the last workload achieved during the $\dot{V}O_{2max}$ test and, if able,

progressed to the next workload. A resting and 3-min post-exhaustive venous blood sample was obtained by venipuncture while the volunteer was sitting for analysis of [La], osmolality ([Osm]), [Hb], Hct, and [RBC]. An arterialized capillary blood sample was also obtained from a warmed fingertip prior to and immediately after the $\dot{V}O_{2max}$ test to assess acid-base status.

Submaximal Whole-Body Endurance Performance.

END_{wb} was assessed on a electromagnetically braked bicycle ergometer. Volunteers warmed-up for 5 min at 60 W. Following warm-up, volunteers began cycling at 40% of their altitude-specific, pre-training $\dot{V}O_{2max}$ for 15 min. The workload was then increased to 70% of their altitude-specific, pre-training $\dot{V}O_{2max}$ for the next 15 min, and then the volunteers, with no rest in between, were asked to perform, as fast as possible, a fixed amount of work consisting of 216 kJ of total work for males and 156kJ of total work for females. This type of submaximal endurance test has been shown to have a high repeatability and low coefficient of variation (47). The bicycle ergometer maintained a constant work rate over a wide range of pedal frequencies (i.e., 40-80 rpm), and could be manually adjusted to increase or decrease the workload in 5 W increments. During this test, the volunteer was informed continuously, by digital read-out, of the total amount of work completed. Time to complete this task was a measure of END_{wb}, and a lower time was considered a better performance. The mean power (W) maintained during the fixed-work portion of the END_{wb} test was calculated as the total work completed during the race divided by the time required to complete the race. The submaximal $\dot{V}O_2$, corresponding to the mean power maintained during the fixed-work portion of the END_{wb} test, was calculated using established equations (2). Volunteers were asked to consume 5 ml water/kg body weight to ensure uniform hydration 1 h before the initiation of the END_{wb} test. An indwelling catheter was placed in an arm vein at least 40 min before the first resting blood sample. Blood samples were drawn after a 40-min sitting equilibration period, at 40% altitude-specific pre-study $\dot{V}O_{2max}$, at 70% altitude-specific pre-study $\dot{V}O_{2max}$, and at exhaustion for measurement of [Hb], Hct, [RBC], [La], [Osm], cortisol concentration ([COR]), norepinephrine concentration ([NOR]), and epinephrine concentration ([EPI]).

Small Muscle Endurance Performance.

END_{sm} was evaluated by measuring the time to exhaustion of the adductor

pollicis muscle during intermittent 5-s static muscle contractions at 50% of rested pre-exercise maximal voluntary contraction (MVC) followed by 5 s of rest. The methods and device used have been described in a previous publication (27).

Blood Sampling and Analysis

Energy substrates were measured 1-4 h after altitude exposure before and after the $\dot{V}O_{2max}$ test and 24-30 h after altitude exposure before and during the END_{wb} test to determine if patterns were consistent with established substrate utilization patterns observed during altitude acclimatization. Aliquots of heparinized blood were used to measure blood [La] in duplicate (Model 2300 YSI analyzer; Yellow Springs Instruments, Yellow Springs, OH). Aliquots of serum were used to measure [Osm] by freezing point depression (Model 2430 Multi-osmette, Precision Systems, Natick, MA). The [RBC] was determined in duplicate using impedance methods (Cell Dyn 3500, Abbott Diagnostic, Abbott Park, IL). Whole blood [Hb] was measured in duplicate by absorbance wavelength (Cell Dyn 3500, Abbott Dianostic, Abbott Park, IL), and Hct was measured using aliquots of heparinized blood and the microcapillary method. [Hb] and Hct determinations were used to calculate changes in plasma volume (23). Arterial oxygen content (CaO_2; $ml \cdot l^{-1}$) was calculated as the product of SaO_2 x [Hb] x 1.34 ml $O_2 \cdot g\ [Hb]^{-1}$.

Metabolic and hematologic hormones were measured ~24-30 h after altitude exposure to determine if patterns were consistent with established patterns observed during altitude acclimatization. Samples were thawed once after storage at -70°C. Serum [COR] was measured using a commercial radioimmunoassay kit (Diagnostic Products Corporation, Los Angeles, CA). Serum [EPO] was measured using a chemiluminescent enzyme immunometric assay (Diagnostic Products Corporation, Los Angeles, CA). The intra-assay coefficients of variation (CV) for [COR] and [EPO] were 5.2% and 3.3%, respectively. All samples for each volunteer were analyzed in duplicate in the same assay to avoid inter-assay variations. Catecholamines were extracted from plasma (Alko Diagnostics Co., Holliston, MA) and measured by high-performance liquid chromatography (Model 2345, Waters Co., Norwell, MA). The percent recovery for the extraction of the catecholamines was 82.0%. The inter- and intra-assay CVs for both [EPI] and [NOR] were less than 3.0% and 2.0%, respectively.

Aliquots of arterialized capillary blood from a pre-warmed finger were collected in

100 μl heparinized capillary tubes, and analyzed immediately for pH, PO_2, and PCO_2 (model ABL 555, Radiometer, Copenhagen). The samples were collected after 1-4 h of altitude exposure prior to and immediately following the $\dot{V}O_{2max}$ test to determine acid-base balance and blood buffering changes associated with altitude acclimatization. Bicarbonate concentration [HCO_3^-] was caculated using the Henderson-Hasselbach equation. Base excess [BE] was calculated from a standard nomogram (97).

STATISTICAL ANALYSIS

Two-way ANOVAs were used to analyze the differences between the independent group factor (PS and ET) and repeated measures altitude factor (SL, PreAc, and PostAc) for dietary measures and 24-h urine volumes, as well as all performance measures during the $\dot{V}O_{2max}$, END_{wb}, END_{sm}, and resting ventilation tests. Three-way ANOVAs with repeated measures on the additional factor of time were used for AMS symptomatology measurements and blood and physiological measurements made during the $\dot{V}O_{2max}$ and END_{wb} tests. Significant main effects and interactions were analyzed using Tukey's least significant difference test. Pearson product-moment correlation coefficients were calculated for relationships between AMS severity and frequency scores calculated from the ESQ and LLS questionnaires. Correlation coefficients were also calculated for AMS sick versus non-sick status and 24-h urine volume and resting ventilation measurements. Statistical significance was set at $P < 0.05$. All data are presented as means ± SD.

RESULTS

All data were examined three ways. First, group (i.e., PS and ET) data were examined to determine whether exercise training enhanced the acclimatization process. Secondly, because of the small number of subjects (n=3) in each group, the groups were combined to examine overall altitude acclimatization effects. Thirdly, individual data were graphed when appropriate to determine whether all individuals followed mean results.

TEST VOLUNTEERS

Mean body weights, heights, energy intakes, 24-h urine volumes, and percent contributions of carbohydrate, fat, and protein to the diet were not different between

groups or testing conditions (Tables 2 and 3). Mean body weight was higher in the PS group compared to the ET group, but was not different between testing conditions in either group. Time spent in physical activity at SL per week was not different between groups, nor changed from baseline values during the 6-wk course of the study.

RESTING VENTILATION

Group and combined group resting ventilation data measured after 24-h exposure to each testing condition are presented in Tables 4 and 5. There were no group differences in any of the resting ventilation parameters in any of the testing conditions. When data from both groups were combined, SaO_2 increased from PreAc to PostAc. Individual, group, and combined group $P_{ET}CO_2$ data are presented in Figure 2. The $P_{ET}CO_2$ decreased 16.6±6.3% in the PS group and 18.4±6.6% in the ET group from SL to PreAc and decreased a further 15.8±3.4% in the PS group from PreAc to PostAc. When data from both groups were combined, $P_{ET}CO_2$ decreased 17.4±5.9% from SL to PreAc and further decreased 11.2±5.9% from PreAc to PostAc.

Table 6 presents the results of comparisons between the change in our mean resting ventilation data from PreAc to PostAc with the mean changes reported from seven chronic altitude residence studies. Ventilatory acclimatization was accomplished anywhere from 50-100% of full ventilatory acclimatization achieved following chronic altitude residence depending on the variable measured. However, this degree of acclimatization was accomplished in ~20% of the total number of hours required to achieve full ventilatory acclimatization.

RESTING HEMATOLOGICAL PARAMETERS

Individual, group, and combined group resting [EPO] data are presented in Figure 3. Resting [EPO] increased in both groups from SL to PreAC and decreased 44.4 ±16.9% in the ET group and 31.5±18.1% in the PS group from PreAc to PostAc. Resting [EPO] at both PreAc and PostAc was higher in the ET group compared to the PS group. When data from both groups were combined, resting [EPO] increased 914±434% from SL to PreAc and then decreased 37.9±17.2% from PreAc to PostAc. At PostAc, resting [EPO] remained approximately 6-fold higher than baseline SL value. Table 7 compares our mean resting [EPO] data with the mean results from six chronic altitude residence studies. The percentage of increase in [EPO] from SL to PreAc was

higher in this intermittent study compared to chronic altitude studies. However, the percentage of decrease in [EPO] from PreAc to PostAc was similar to [EPO] results from chronic altitude studies. However, due to the large acute increase in [EPO] at PreAc, the [EPO] value at PostAc compared to baseline SL value was much higher in this intermittent study compared to chronic altitude studies.

Resting values for [Hb], Hct, [RBC], and PV changes are presented in the appropriate tables during the conduct of the VO_{2max} and END_{wb} tests. Table 8 compares our mean resting percentage of change in [Hb], Hct, and PV from SL to PreAc and PostAc with the results from nine chronic altitude residence studies. The percentages of change for [Hb] or Hct and PV from SL to PreAc were similar between this intermittent study and chronic altitude studies. However, unlike chronic altitude residence, PV did not continue to decrease nor did [Hb] continue to increase with continued intermittent exposures. The percentage of change in [Hb] and PV with 15 d of intermittent altitude exposure was ~35% of the values achieved following chronic altitude residence.

ACUTE MOUNTAIN SICKNESS SYMPTOMATOLOGY

Group and combined group AMS-C, AMS-R, Lake Louise self-report, and Lake Louise self-report plus clinical symptom severity scores are presented in Tables 9 and 10. Both Lake Louise scores increased in the ET group at 24-h PreAc compared to 24-h SL and decreased at 24-h PostAc compared to 24-h PreAc. No other group differences were present. When both groups were combined, 12-h AMS-C increased from SL to PreAc and decreased at 12-h PostAc. The 24-h and 30-h Lake Louise self-report increased at PreAc compared to SL and decreased at 24-h and 30-h PostAc. There were no group differences in AMS frequency between the PS (1 sick) and ET (2 sick) groups. The combined group AMS frequency scores determined by both the ESQ and Lake Louise assessments are presented in Figure 4. The AMS frequency assessed by both the Lake Louise and ESQ were increased at 24-h and 30-h PreAc compared to SL and decreased at 24-h and 30-h PostAc compared to PreAc. The AMS frequency was identical for both the Lake Louise and ESQ for all time points ($r=1.0$). The AMS ESQ-C and Lake Louise self-report severity scores were correlated at PreAc at 6-h ($r=0.89$; $p=0.02$), 12-h ($r=0.95$; $p=0.003$), 24-h ($r=0.92$; $p=0.009$), and 30-h ($r=0.93$; $p=0.008$). AMS sick versus non-sick status at PreAc was correlated with 24-h urine volume at PreAc2 ($r=0.98$; $p<0.05$) and resting SaO_2 at PreAc2 ($r=0.99$;

$p<0.01$), but not with resting $P_{ET}CO_2$ at PreAc2. Significant differences existed for sick versus non-sick individuals and 24-h urine volume and resting SaO_2 at PreAc2 (Figure 5).

Table 11 compares our mean AMS-C frequency and severity data after 12-24 h altitude exposure at PreAc and PostAc with the mean results from six chronic altitude residence studies. The severity and frequency scores upon both acute and chronic altitude exposure are similar between this intermittent study and the chronic altitude residence studies. Similar to chronic altitude residence, 15 d of intermittent altitude exposure resulted in full elimination of AMS-C symptoms.

MAXIMAL EXERCISE PERFORMANCE

Individual, group, and combined group $\dot{V}O_{2max}$ data are presented in Figure 6. There were no group differences in $\dot{V}O_{2max}$ in any of the testing conditions. However, when data from both groups were combined, $\dot{V}O_{2max}$ decreased 22.0±% from SL to PreAc and increased 18.0±% from PreAc to PostAc. The percentage of the initial decrease in $\dot{V}O_{2max}$ from SL to PreAc regained from PreAc to PostAc was 45.6±57.8% and 59.9±4.4% in the PS and ET groups, respectively, and 52.7±37.5% when data from both groups were combined. The percentage of $\dot{V}O_{2max}$ regained did not differ between groups. Group maximal RPE values did not differ between groups or testing conditions. Combined group maximal RPE values at SL (18.8±1.2), PreAc (17.7±1.5), and PostAc (18.3±1.2) were not different.

Table 12 compares our mean $\dot{V}O_{2max}$ data at SI, PreAC, and PostAc with the mean results from six chronic altitude residence studies. The percentage of decrease in $\dot{V}O_{2max}$ from SL to PreAc was similar in both this intermittent study and upon acute altitude exposure. However, the large ~18% increase in $\dot{V}O_{2max}$ from PreAc to PostAc was dramatically different from the ~0% change reported following chronic altitude residence.

Group and combined group resting and maximal ventilatory parameters are presented in Tables 13 and 14. Maximal $\dot{V}_E$ increased in both groups from PreAc to PostAc. Resting $\dot{V}_E \cdot \dot{V}CO_2^{-1}$ also increased in the PS group from PreAc to PostAc. Otherwise, there were no group changes in ventilatory parameters from PreAc to PostAc. However, when data from both groups were combined, maximal $\dot{V}O_2$, $\dot{V}_E$,

$\dot{V}E \cdot \dot{V}CO_2^{-1}$, and SaO_2 increased from PreAc to PostAc.

Group and combined group resting and maximal cardiovascular parameters are presented in Tables 15 and 16. Maximal CaO_2 increased in both groups from PreAc to PostAc. None of the other group cardiovascular parameters increased from PreAc to PostAc. When data from both groups were combined, maximal DBP, MAP, O_2 Pulse, and CaO_2 increased from PreAc to PostAc. Combined group resting CaO_2 also increased from PreAc to PostAc.

Group and combined group resting and maximal metabolic and hematologic parameters are presented in Tables 17 and 18. There were no group changes in any of these parameters from PreAc to PostAc. When both groups were combined, [Hb] increased from PreAc to PostAc. The percentage of change in PV from SL to PreAc in the PS group (3.7±9.8) and ET group (1.9±9.2) were not different. The percentage of change in PV from PreAc to PostAc in the PS group (-1.9±7.3) and ET group (-1.3±11.7) were also not different. When data from both groups were combined, the percentage of change in PV from SL to PreAc (2.8±8.6%) and from PreAc to PostAc (-1.6±8.7%) was not different.

Group and combined group resting and maximal acid-base parameters are presented in Tables 19 and 20. The maximal pH was decreased from PreAc to PostAc in the PS group only. Group resting and maximal PO_2 remained unchanged from PreAc to PostAc. Both resting and maximal PCO_2 and $[HCO_3^{-1}]$ were decreased from PreAc to PostAc in both groups. When data from both groups were combined, maximal pH was decreased, resting and maximal PO_2 remained unchanged, resting and maximal PCO_2 were decreased, and resting and maximal $[HCO_3^{-1}]$ were decreased from PreAc to PostAc.

SUBMAXIMAL WHOLE-BODY ENDURANCE PERFORMANCE

Individual, group and combined group END_{wb} data are presented in Figure 7. There were no group differences in END_{wb} time in any of the testing conditions. When data from both groups were combined, END_{wb} time increased 61.4±34.7% from SL to PreAc and decreased 20.6±15.9% from PreAc to PostAc. The percentage of improvement in END_{wb} time from PreAc to PostAc was positively correlated with the percent improvement in $\dot{V}O_{2max}$ from PreAc to PostAc (r=0.99; p=0.0001). The

percentage of the initial increase in END_{wb} time from SL to PreAc regained from PreAc to PostAc was 34.1±22.6% and 64.3±20.0% in the PS and ET groups, respectively, and 49.2±42.4% when data from both groups were combined. The percentage of END_{wb} time regained did not differ between groups. Group mean RPE values collected at rest, 40% of altitude-specific pre-training $\dot{V}O_{2max}$, 70% of altitude-specific pre-training $\dot{V}O_{2max}$, and at exhaustion during the END_{wb} test were not different between groups or testing conditions. Combined group RPE values collected at exhaustion during the END_{wb} test at SL (16.5±2.3), PreAc (17.0±1.9), and PostAc (16.7±1.6) did not differ.

Group and combined group submaximal fixed-work $\dot{V}O_2$ data measured during the END_{wb} test are presented in Figure 8. The submaximal fixed-work $\dot{V}O_2$ decreased from SL to PreAc, but remained the same from PreAc to PostAc in both groups. There were no group differences in submaximal fixed-work $\dot{V}O_2$ data. When data from both groups were combined, submaximal fixed-work $\dot{V}O_2$ decreased 31.6±12.1% from SL to PreAc and did not change from PreAc to PostAc. The percentage of altitude-specific $\dot{V}O_{2max}$ maintained during the fixed-work portion of the END_{wb} test data are presented in Figure 9. There were no differences in the percentage of altitude-specific $\dot{V}O_{2max}$ maintained in any of the testing conditions in either group. When data from both groups were combined, the percentage of altitude-specific $\dot{V}O_{2max}$ maintained during the fixed-work portion of the END_{wb} test decreased 14.8±10.2% from SL to PreAc but did not change from PreAc to PostAc.

Group and combined group ventilatory parameters, measured at rest, 40% of altitude-specific pre-training $\dot{V}O_{2max}$, and 70% of altitude-specific pre-training $\dot{V}O_{2max}$, during the END_{wb} test are presented in Tables 21 and 22. Resting and 70% SaO_2 increased in the ET group from PreAc to PostAc. Otherwise, there were no group changes in ventilatory parameters from PreAc to PostAc. However, when data from both groups were combined, resting $\dot{V}E \cdot \dot{V}O_2^{-1}$, $\dot{V}E \cdot \dot{V}CO_2^{-1}$, and SaO_2 increased from PreAc to PostAc, and 40% SaO_2 increased from PreAc to PostAc.

Group and combined group cardiovascular parameters, measured at rest, 40% of altitude-specific pre-training $\dot{V}O_{2max}$, 70% of altitude-specific pre-training $\dot{V}O_{2max}$, and at exhaustion during the END_{wb} test are presented in Tables 23 and 24. Resting, 40%, and 70% HR were decreased from PreAc to PostAc in the ET group, while resting and 40% CaO_2 were increased from PreAc to PostAc in the ET group. When data from

both groups were combined, resting, 40%, and exhaustion CaO_2 increased from PreAc to PostAc.

Group and combined group hematologic parameters, measured at rest, 40% of altitude-specific pre-training VO_{2max}, 70% of altitude-specific pre-training VO_{2max}, and at exhaustion during the END_{wb} test are presented in Tables 25 and 26. [EPO] increased from SL to PreAc at all four time points in both groups, then decreased from PreAc to PostAc at all four time points in both groups. There were no group changes in any other hematologic parameters from PreAc to PostAc. When both groups were combined, there were still no changes in any of the hematologic parameters except [EPO]. The percentage of change in plasma volume from SL to PreAc in the PS group (-10.3±4.0) and ET group (-7.5±3.9) were not different. The percentage of change in plasma volume from PreAc to PostAc in the PS group (3.7±3.5) and ET group (1.1±12.3) were also not different. When data from both groups were combined, the percentage of change in plasma volume from SL to PreAc (-8.9±3.9%) and from PreAc to PostAc (2.4±8.2%) was not different.

Group and combined group metabolic and hormonal parameters measured at rest, 40% of altitude-specific pre-training VO_{2max}, 70% of altitude-specific pre-training VO_{2max}, and at exhaustion during the END_{wb} test are presented in Tables 27 and 28. There were no group or combined group changes in [EPI], [NOR], or [COR] at any time point during the END_{wb} test. Combined group [La] was lower at PostAc compared to PreAc at 70% of altitude-specific pre-training VO_{2max}.

SUBMAXIMAL SMALL-MUSCLE ENDURANCE PERFORMANCE

Individual, group, and combined group END_{sm} data are presented in Figure 10. There were no group differences in END_{sm} time or MVC in any of the testing conditions. When data from both groups were combined, END_{sm} time increased 64.5±57.3% from PreAc to PostAc. The percentage of the initial decrease in END_{sm} from SL to PreAc regained from PreAc to PostAc was 118.6±37.5% when data from both groups were combined. The MVC at SL (31.6±9.6), PreAc (29.2±9.0), and PostAc (28.8±7.6) were not different.

Table 29 compares our mean END_{sm} data at SL, PreAC, and PostAc with the mean results from three chronic altitude residence studies. The percentage of

decrease in END_{sm} from SL to PreAc was similar in both this intermittent study and upon acute altitude exposure. However, the 64.5% increase in END_{sm} from PreAc to PostAc was larger than the 33% change reported following chronic altitude residence. Thus, the 138% regain in END_{sm} from PreAc to PostAc was larger than the 118% regain reported in chronic altitude residence studies. The percentage of acclimatization achieved after 15 d of intermittent altitude exposure for END_{sm} was greater than 100% of that achieved following chronic altitude residence.

TRAINING DAYS

Combined group resting HR, SaO_2, and MAP collected every other day during intermittent altitude exposures are presented in Figure 11. SaO_2 increased from Day 1 of training to Day 15 of training. The other variables did not change from Day 1 to Day 15 of training.

Table 2. Group Body Weight, Height, 24-h Urine Volume, Energy Intake, and Percentage (%) Contribution of Carbohydrate, Fat, and Protein to the Diet.

Con-dition	Body weight (kg)		Height (cm)		Urine Volume Day 1 ($ml \cdot 24h^{-1}$)		Urine Volume Day 2 ($ml \cdot 24h^{-1}$)		Energy Intake (kcal)		% Carbo-hydrate		% Fat		% Protein	
	PS	ET	PS	ET	PS	ET	PS	ET	PS	ET	PS	ET	PS	ET	PS	ET
SL	79.1 ±12.6	75.7 ±18.3‡	175 ±11	179 ±6	1858 ±831	1317± 724	2108 ±546	992 ±332	2831 ±614	2800 ±293	59 ±10	56 ±6	24 ±9	32 ±9	17 ±11	12 ±2
Pre Ac	79.5 ±13.6	75.6 ±18.3‡	175 ±11	179 ±6	2750 ±1719	2067 ±1533	1427 ±762	1750 ±1085	2297 ±343	1408 ±532	58 ±6	55 ±16	28 ±4	32 ±6	14 ±4	12 ±4
Post Ac	79.1 ±11.2	75.2 ±18.4‡	175 ±11	179 ±6	3666 ±1150	867 ±431	2083 ±664	1533 ±462	1820 ±463	2450 ±1009	54 ±7	55 ±6	34 ±6	34 ±7	12 ±6	11 ±1

Mean ±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET).

Table 3. Combined Group Body Weight, Height, 24-h Urine Volume, Energy Intake, and Percentage (%) Contribution of Carbohydrate, Fat, and Protein to the Diet.

Con-Dition	Body weight (kg)	Height (cm)	Urine Volume Day 1 ($ml \cdot 24h^{-1}$)	Urine Volume Day 2 ($ml \cdot 24h^{-1}$)	Energy Intake (kcal)	% Carbohydrate	% Fat	% Protein
SL	77.4±14.2	177±8	1587±758	1550±733	2815±475	58±8	28±8	14±8
PreAc	77.5±14.6	177±8	2408±1504	1588±867	1853±631	56±11	31±9	13±3
PostAc	77.1±13.8	177±8	2267±1719	1808±594	2135±319	55±6	34±4	11±4

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc).

Table 4. Group Resting Ventilation Measurements.

Condition	$\dot{V}O_2$ ($l \cdot min^{-1}$)		$\dot{V}E$ ($l \cdot min^{-1}$)		$\dot{V}E \cdot \dot{V}O_2^{-1}$		$\dot{V}E \cdot \dot{V}CO_2^{-1}$		SaO_2 (%)		RER	
	PS	ET	PS	ET	PS	ET	PS	ET	PS	ET	PS	ET
SL	0.25 ±0.03	0.21 ±0.03	8.8 ±0.7	8.8 ±0.7	36.1 ±1.5	41.7 ±4.5	38.0 ±4.6	46.8 ±3.6	98 ±2	99 ±1	0.92 ±0.09	0.88 0.02
PreAc	0.26 ±0.01	0.24 ±0.08	11.6 ±0.9*	11.9 ±1.7*	49.6 ±4.9	69.2 ±25.2	45.2 ±3.0	58.8 ±12.1‡	81 ±8*	79 ±4*	1.00 ±0.02	0.91 0.07
PostAc	0.26 ±0.04	0.21 ±0.06	12.1 ±0.7*	12.4 ±2.4*	52.6 ±12.0	67.7 ±12.9	50.9 ±6.8*	62.1 ±7.7*	85 ±4*	86 ±2*	0.93 ±0.05	0.97 0.06

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET), Oxygen uptake ($\dot{V}O_2$), Minute ventilation ($\dot{V}E$), Ventilatory equivalent for oxygen ($\dot{V}E \cdot \dot{V}O_2^{-1}$), Ventilatory equivalent for carbon dioxide ($\dot{V}E \cdot \dot{V}CO_2^{-1}$), Arterial oxygen saturation (SaO_2), Respiratory exchange ratio (RER).

Table 5. Combined Group Resting Ventilation Measurements.

Condition	$\dot{V}O_2$ ($l \cdot min^{-1}$)	$\dot{V}E$ ($l \cdot min^{-1}$)	$\dot{V}E \cdot \dot{V}O_2^{-1}$	$\dot{V}E \cdot \dot{V}CO_2^{-1}$	SaO_2 (%)	RER
SL	0.23±0.03	8.8±0.6	38.9±4.3	42.5±6.1	99±1	0.90±0.04
PreAc	0.25±0.05	11.7±1.2*	59.4±19.4*	52.0±10.8*	80±6*	0.96±0.06
PostAc	0.24±0.05	12.2±1.6*	60.2±13.9*	56.5±8.9*	85±3*†	0.95±0.05

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc), Oxygen uptake ($\dot{V}O_2$), Minute ventilation ($\dot{V}E$), Ventilatory equivalent for oxygen ($\dot{V}E \cdot \dot{V}O_2^{-1}$), Ventilatory equivalent for carbon dioxide ($\dot{V}E \cdot \dot{V}CO_2^{-1}$), Arterial oxygen saturation (SaO_2), Respiratory exchange ratio (RER).

Table 6. Comparison of the Change in our Mean Resting Ventilation Data from Pre-to Post-Acclimatization with the Mean Results from Ten Chronic Altitude Residence Studies.

Study	Altitude (m)	Days	Hours	ΔPaO_2 (mmHg)	ΔSaO_2 (%)	$\Delta \dot{V}E \cdot \dot{V}CO_2^{-1}$	ΔpH	$\Delta PaCO_2$ (mmHg)	$\Delta[HCO_3^-]$ (mM)
(115)	4,300	9	216	6.0	6.0		0.000	-5.0	
(20)	4,350	10	240	6.1			0.044	-4.5	
(40,41)	4,300	14	336	10.0	5.5		0.006	-3.3	-2.7
(39)	4,300	14	336	9.0	10.0		0.040	-6.0	-2.5
(26)	4,300	11	264	6.0			0.020	-6.0	-5.0
(57)	4,509	4	96	5.5	8.0		0.015	-4.7	-2.5
(78)	4,300	19	456		7.0				
(71)	4,300	14	336		10.0	6.0			
(67)	4,300	19	456		13.0	9.0			
Mean (Chronic Studies)	**4,328**	**12.7**	**304**	**7.1**	**8.5**	**7.5**	**0.02**	**-4.9**	**-3.2**
Mean (This Study)	**4,300**	**15**	**60**	**4.7**	**5.0**	**4.5**	**0.01**	**-4.9**	**-3.2**
% of Chronic Response			**19.7**	**66.2**	**58.9**	**60.0**	**50.0**	**100.0**	**100.0**

partial pressure of arterial oxygen (PaO_2); arterial oxygen saturation (SaO_2); ventilatory equivalent for carbon dioxide ($\Delta \dot{V}E \cdot \dot{V}CO_2^{-1}$;partial pressure of arterial carbon dioxide ($PaCO_2$); % of Chronic Response (Mean This Study/Mean Chronic Studies).

Table 7. Comparison of the Change in our Mean Resting Erythropoietin [EPO] from PreAc to PostAc with the Results Observed upon Acute Altitude (AA) and Chronic Altitude (CA) Exposure Compared to Sea Level (SL) in Six Chronic Altitude Residence Studies.

Study	Altitude (m)	Days	Hours	[EPO] SL ($\mu U \cdot l^{-1}$)	[EPO] AA ($\mu U \cdot l^{-1}$)	[EPO] CA ($\mu U \cdot l^{-1}$)	% Change [EPO (SL-AA)	% Change [EPO] (AA-CA)	% Change [EPO] (SL-CA)
(1)	4,359	10	240	3	22	5	633	-77	67
(96)	4,300	9	216	11	29	17	164	-41	55
(61)	4,559	5	120	17	67	25	294	-65	47
(65)	4,500	22	528	25	68	35	172	-49	40
(34)	4,300	20	480	17	21	22	24	+5	29
(53)	4,350	4	96	6	58	31	867	-46	417
Mean (Chronic Studies)	**4,394**	**11.7**	**280**	**13**	**44**	**23**	**238**	**-48**	**77**
Mean (This Study)	**4,300**	**15**	**60**	**9**	**92**	**54**	**922**	**-41**	**+500**
% of Chronic Response			**21.4**	**N/A**	**N/A**	**N/A**	**N/A**	**85**	**649**

% Chronic Response (Mean This Study/Mean Chronic Studies)

Table 8. Comparison of the Percentage of Change in Our Mean Resting Hemoglobin ([Hb]), Hematocrit (Hct), and Plasma Volume (PV) from PreAc to PostAc with the Results Observed upon Acute Altitude (AA) and Chronic Altitude (CA) Exposure Compared to Sea Level (SL) in Nine Chronic Altitude Residence Studies.

Study	Altitude (m)	Hours	% Change [Hb] or Hct (SL-AA) (1-4 h)	% Change [Hb] or Hct (SL-AA) (1-4 d)	% Change [Hb] or Hct (SL-CA) (5-10 d)	% Change [Hb] or Hct (SL-CA) (11-21 d)	% Change PV (SL-AA) (1-4 h)	% Change PV (SL-AA) (1-4 d)	% Change PV (SL-CA) (5-10 d)	% Change PV (SL-CA) (11-21 d)
(10)	4,300	384	+0.6			+15.1	-2.6			-26.1
(32)	4,300	336	-2.8		+9.7	+14.5	+4.6		-12.7	-21.2
(113)	4,300	504	+1.5			+13.2	-11.3			-18.2
(34)	4,300	480			+6.4	+12.1			-6.4	-14.5
(96)	4,300	264		+4.0	+6.3			-8.4	-9.0	
(60)	4,300	264		+5.8		+12.8		-5.6		-17.5
(101)	4,300	192						-13.2		-19.6
(39)	4.300	360		+1.4	+3.4	+4.7		-9.3	-13.3	-19.3
(68)	4,300	456		+9.3	+22.0	+23.3				
Mean (Chronic Studies)	**4,300**	**360**	**+0.5**	**+4.8**	**+9.6**	**+16.2**	**-3.1**	**-9.1**	**-10.4**	**-19.5**
Mean (This Study)	**4,300**	**60**	**-1.4**	**+6.4**		**+5.7**	**+2.8**	**-8.9**		**-6.8**
% of Chronic Response		**16.8**	**N/A**	**N/A**		**35.2**	**N/A**	**N/A**		**34.9**

% Chronic Response (Mean This Study/Mean Chronic Studies)

Table 9. Group Acute Mountain Sickness (AMS) Severity Scores Measured at Different Time Points During a 30-h Altitude Exposure.

Condition	Time	AMS-C		AMS-R		Lake Louise (Self-Report)		Lake Louise (Self-Report + Clinical)	
		PS	ET	PS	ET	PS	ET	PS	ET
SL	6h	0.00±0.00	0.05±0.09	0.00±0.00	0.04±0.07	0.33±0.58	0.67±0.58	0.33±0.58	0.67±0.58
	12h	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.67±0.58	0.00±0.00	0.67±0.58
	24h	0.00±0.00	0.00±0.00	0.00±0.00	0.06±0.11	0.33±0.58	0.00±0.00	0.33±0.58	0.00±0.00
	30h	0.00±0.00	0.03±0.05	0.00±0.00	0.06±0.08	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
PreAC	6h	0.06±0.10	0.56±0.43	0.00±0.00	0.36±0.32	1.00±1.73	3.00±1.73	2.33±3.21	3.33±1.53
	12h	0.81±0.00	0.70±0.76	0.10±0.14	0.30±0.26	2.67±3.78	2.67±2.51	3.00±4.36	3.67±2.52
	24h	0.20±0.35	0.78±0.40	0.09±0.08	0.26±0.32	3.00±1.00	5.33±2.88*	3.67±2.08	6.67±3.21*
	30h	0.40±0.44	0.63±0.51	0.19±0.34	0.33±0.20	3.33±3.21	4.00±2.00	3.67±4.04	4.33±2.51*
PostAc	6h	0.02±0.04	0.05±0.05	0.05±0.08	0.09±0.15	0.33±0.58	0.67±1.15	0.33±0.58	0.67±1.15
	12h	0.00±0.00	0.06±0.11	0.00±0.00	0.06±0.07	0.00±0.00	0.67±0.58	0.00±0.00	0.67±0.58
	24h	0.00±0.00	0.02±0.04	0.00±0.00	0.03±0.06	0.67±0.58	1.00±1.00†	0.67±0.58	1.00±1.00†
	30h	0.00±0.00	0.03±0.04	0.24±0.42	0.00±0.00	0.33±0.58	0.67±1.15	0.00±0.00	0.67±1.15

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET); 4-h post-exposure (4h); 12-h post-exposure (12h); 24-h post-exposure (24h); 30-h post-exposure (30h), Acute mountain sickness cerebral score (AMS-C), acute mountain sickness respiratory score (AMS-R).

Table 10. Combined Group Acute Mountain Sickness (AMS) Severity Scores Measured at Different Time Points During a 30-h Altitude Exposure.

Condition	Time	AMS-C	AMS-R	Lake Louise (Self-Report)	Lake Louise (Self-Report + Clinical)
SL	6h	0.02±0.06	0.02±0.05	0.50±0.55	0.50±0.55
	12h	0.00±0.00	0.00±0.00	0.33±0.52	0.33±0.52
	24h	0.00±0.00	0.03±0.07	0.17±0.41	0.17±0.41
	30h	0.14±0.03	0.03±0.06	0.00±0.00	0.00±0.00
Pre Ac	6h	0.31±0.39	0.18±0.28	2.00±1.89	2.83±2.32
	12h	0.75±0.97*	0.20±0.22	2.67±2.87	3.33±3.20*
	24h	0.49±0.46	0.17±0.23	4.16±2.31*	5.17±2.93*
	30h	0.52±0.45	0.26±0.26	3.67±2.42*	4.00±3.03*
Post Ac	6h	0.04±0.04	0.07±0.11	0.50±0.84	0.50±0.84
	12h	0.03±0.07†	0.03±0.06	0.33±0.52	0.33±0.52†
	24h	0.01±0.03	0.02±0.04	0.83±0.75†	0.83±0.75†
	30h	0.01±0.03	0.12±0.29	0.50±0.84†	0.33±0.82†

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); 4-h post-exposure (4h); 12-h post-exposure (12h); 24-h post-exposure (24h); 30-h post-exposure (30h), Acute Mountain Sickness Cerebral score (AMS-C), Acute Mountain Sickness Respiratory score (AMS-R).

Table 11. Comparison of the Change in our Mean Resting AMS-C Severity and Frequency Data from PreAc to PostAc with the Results Observed upon Acute Altitude (AA) and Chronic Altitude (CA) exposure in Four Chronic Altitude Residence Studies.

Study	Altitude (m)	Days	Hours	AA AMS-C (12-24 h)	CA AMS-C (6-19 d)	Δ AMS-C (AA-CA)	AA AMS Frequency (%)	CA AMS Frequency (%)
(84)	4,300	6	144	0.79	0.02	0.77	50	0
(31)	4,300	19	456	1.11	0.03	1.08	N/A	N/A
(59)	4,300	16	384	0.61	0.03	0.58	67	0
(85)	4,300	12	288	0.65	0.01	0.64	46	0
Mean (Chronic Studies)	**4,300**	**13.2**	**318**	**0.79**	**0.02**	**0.77**	**54**	**0**
Mean (This Study)	**4,300**	**15**	**60**	**0.75**	**0.03**	**0.72**	**50**	**0**
% of Chronic Response			**18.9**	**N/A**	**N/A**	**93.5**	**N/A**	**100.0**

% Chronic Response (Mean This Study/Mean Chronic Studies), Acute Mountain Sickness Cerebral score (AMS-C).

Table 12. Comparison of the Change in our VO_{2max} Data from PreAc to PostAc with the Results Observed upon Acute Altitude (AA) and Chronic Altitude (CA) Exposure Compared to Sea Level (SL) in Six Chronic Altitude Residence Studies.

Study	Altitude (m)	Days	Hours	SL VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$)	AA VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$)	CA VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$)	Δ VO_{2max} (AA-CA) ($ml \cdot kg^{-1} \cdot min^{-1}$)	% Change (SL-AA)	% Change (AA-CA)
(89)	4,300	14	336	49.9	35.4	34.3	-1.1	-29.1	-3.1
(105)	4,350	10	240	44.6	35.1	33.0	-1.9	-21.3	-5.9
(114)	4,300	18	432	44.9	32.8	32.3	-0.5	-26.9	-1.5
(68)	4,300	19	456	45.5	33.7	33.2	-0.5	-26.0	-1.5
(32)	4,300	14	336	50.1	37.2	39.4	+2.2	-26.0	5.9
(113)	4,300	21	504	49.3	37.4	37.7	+0.3	-23.5	0.8
(115)	4,300	9	216	52.2	37.4	40.0	+2.6	-28.3	6.9
Mean (Chronic Studies)	**4,300**	**15.0**	**360**	**48.1**	**35.6**	**35.7**	**+0.2**	**-25.9**	**+0.2**
Mean (This Study)	**4,300**	**15**	**60**	**45.1**	**34.8**	**40.7**	**+5.9**	**-22.8**	**17.9**
% of Chronic Response			**16.7**	**N/A**	**N/A**	**N/A**	**2950**	**N/A**	**8950**

% Chronic Response (Mean This Study/Mean Chronic Studies)

Table 13. Group Resting and Maximal Ventilatory Parameters.

Condition	Time	VO_2 ($l \cdot min^{-1}$)		$\dot{V}E$ ($l \cdot min^{-1}$)		$\dot{V}E \cdot VO_2^{-1}$		$\dot{V}E \cdot VCO_2^{-1}$		SaO_2 (%)		RER	
		PS	ET	PS	ET	PS	ET	PS	ET	PS	ET	PS	ET
SL	Rest	0.31 ±0.06	0.24 ±0.09	11 ±4	9 ±2	34.9 ±5.4	38.3 ±6.2	42.5 ±3.6	43.3 ±5.9	98 ±1	98 ±1	0.82 ±0.05	0.89 ±0.14
	Max	3.58 ±0.36	3.26 ±1.04	146 ±36	127 ±32	40.4 ±3.2	39.9 ±3.9	36.6 ±3.1	36.5 ±1.1	97 ±2	98 ±2	1.11 ±0.07	1.10 ±0.10
Pre Ac	Rest	0.36 ±0.03	0.35 ±0.07	14 ±2	13 ±2	39.6 ±4.2	37.7 ±0.9	36.2 ±3.9	40.6 ±4.9	84 ±7*	80 ±4*	0.97 ±0.12	0.90 ±0.08
	Max	3.07 ±0.85	2.38 ±0.59*‡	159 ±46	128 ±26‡	51.7 ±4.6*	54.4 ±3.1*	47.3 ±4.6*	45.9 ±4.8	72 ±7*	69 ±7*	1.10 ±0.04	1.19 ±0.07
Post Ac	Rest	0.40 ±0.07	0.36 ±0.03	17 ±3	15 ±2	43.2 ±0.7*	40.5 ±1.2	50.1 ±2.8†	47.5 ±4.4	88 ±4	86 ±2*	0.86 ±0.04	0.86 ±0.10
	Max	3.40 ±0.59	2.92 ±0.88	191 ±36*†	172 ±45*†	56.1 ±2.7*	59.6 ±2.9*	55.8 ±5.3*	55.7 ±0.8*	79 ±6*	77 ±9*	1.01 ±0.06	1.07 ±0.04

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET), Oxygen uptake (VO_2), Minute ventilation ($\dot{V}E$), Ventilatory equivalent for oxygen ($\dot{V}E \cdot VO_2^{-1}$), Ventilatory equivalent for carbon dioxide ($\dot{V}E \cdot VCO_2^{-1}$), Arterial oxygen saturation (SaO_2), Respiratory exchange ratio (RER).

Table 14. Combined Group Resting and Maximal Ventilatory Parameters.

Condition	Time	$\dot{V}O_2$ ($l \cdot min^{-1}$)	$\dot{V}E$ ($l \cdot min^{-1}$)	$\dot{V}E \cdot \dot{V}O_2^{-1}$	$\dot{V}E \cdot \dot{V}CO_2^{-1}$	SaO_2 (%)	RER
SL	Rest	0.27±0.08	10±32	36.6±5.5	42.9±4.4	98±1	0.85±0.10
	Max	3.42±0.83	136±32	40.2±3.2	36.5±2.1	98±2	1.10±0.08
Pre Ac	Rest	0.36±0.05	14±2	38.6±2.9	38.4±4.6	82±7*	0.94±0.10
	Max	2.73±0.75*	144±37	53.0±3.8*	46.6±4.3*	70±7*	1.14±0.07
Post Ac	Rest	0.38±0.05	16±2	41.8±1.7	48.8±3.6	87±3*	0.86±0.07
	Max	3.16±0.72†	182±38*†	57.8±3.2*	55.7±3.4*†	78±7*†	1.04±0.05

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc), Oxygen uptake ($\dot{V}O_2$), Minute ventilation ($\dot{V}E$), Ventilatory equivalent for oxygen ($\dot{V}E \cdot \dot{V}O_2^{-1}$), Ventilatory equivalent for carbon dioxide ($\dot{V}E \cdot \dot{V}CO_2^{-1}$), Arterial oxygen saturation (SaO_2), Respiratory exchange ratio (RER).

Table 15. Group Resting and Maximal Cardiovascular Parameters.

Condition	Time	HR (beats•min^{-1})		SBP (mmHg)		DBP (mmHg)		MAP (mmHg)		O_2 Pulse (ml•beat^{-1})		CaO_2 (ml O_2•l^{-1})	
		PS	ET	PS	ET	PS	ET	PS	ET	PS	ET	PS	ET
SL	Rest	72 ±5	75 ±8	108 ±14	128 ±19	67 ±7	60 ±14	81 ±8	83 ±4	4 ±1	3 ±1	196 ±11	193 ±20
	Max	192 ±14	189 ±17	144 ±13	152 ±11	74 ±14	87 ±25	98 ±5	109 ±15	19 ±2	18 ±7	213 ±13	210 ±16
Pre Ac	Rest	80 ±5	87 ±12	116 ±8	102 ±2	66 ±2	63 ±2	82 ±7	76 ±6	4 ±1	4 ±1	166 ±19*	154 ±16*
	Max	178 ±10	181 ±14	142 ±4	144 ±11	72 ±3	74 ±5	96 ±3	97 ±7	17 ±4	13 ±4	142 ±23*	132 ±7*
Post Ac	Rest	73 ±2	84 ±5	120 ±10	127 ±22	66 ±9	60 ±10	84 ±6	82 ±4	6 ±1	4 ±1	177 ±12	171 ±20*
	Max	171 ±6*	182 ±10	145 ±3	140 ±14	95 ±25	96 ±26	112 ±17	110 ±18	20 ±2	16 ±5	171 ±13*†	163 ±14*†

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), arterial oxygen content (CaO_2).

Table 16. Combined Group Resting and Maximal Cardiovascular Parameters.

Condition	Time	HR (beats•min^{-1})	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	O_2 Pulse (ml•beat^{-1})	CaO_2 (ml O_2•l^{-1})
SL	Rest	73±6	118±18	64±11	82±6	4±1	194±15
	Max	190±14	148±12	81±19	103±12	18±5	212±13
Pre Ac	Rest	84±9*	109±9	64±3	79±7	4±1	160±15*
	Max	180±11*	143±8	73±4	96±5	15±4*	137±16*
Post Ac	Rest	79±7	123±16	63±9	83±4	5±1	174±16*†
	Max	176±9*	142±9	95±23*†	111±16†	18±5†	167±13*†

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), arterial oxygen content (CaO_2).

Table 17. Group Resting and Maximal Metabolic and Hematologic Parameters.

Condition	Time	[La] ($mM \cdot l^{-1}$)		[Osm] (osmol•kg H_2O^{-1})		[Hb] ($g \cdot dl^{-1}$)		Hct (%)		[RBC] ($10^6 \cdot \mu l^{-1}$)		Plasma Volume (% Change from Rest)	
		PS	ET	PS	ET	PS	ET	PS	ET	PS	ET	PS	ET
SL	Rest	2.0 ±1.2	1.4 ±0.5	285.3 ±6.1	290.0 ±1.0	14.8 ±0.9	14.4 ±1.5	48.3 ±2.7	45.4 ±4.0‡	5.1 ±0.3	4.8 ±0.4‡		
	Max	16.3 ±2.5	12.7 ±2.4	294.3 ±4.5	292.7 ±4.0	16.1 ±0.7	15.8 ±1.4	52.3 ±1.8	50.2 ±4.1	5.5 ±0.2	5.2 ±0.4‡	-15.5 ±3.0	-16.8 ±2.2
Pre Ac	Rest	1.8 ±0.4	2.1 ±0.5	283.7 ±2.1	284.0 ±3.6	14.6 ±0.9	14.2 ±0.8	47.3 ±1.7	45.0 ±1.9	5.0 ±0.0	4.8 ±0.2		
	Max	14.5 ±3.9	10.8 ±3.3	292.3 ±3.2	290.3 ±1.2	15.6 ±0.6*	15.3 ±0.7*	50.6 ±0.9	48.5 ±1.3	5.3 ±0.1	5.1 ±0.2	-12.3 ±4.2	-12.8 ±2.0
Post Ac	Rest	4.6 ±1.1	2.0 ±0.1	287.3 ±5.8	284.7 ±0.6	14.8 ±0.5	14.6 ±1.7	47.4 ±1.0	44.7 ±5.0	5.0 ±0.1	4.8 ±0.4‡		
	Max	16.4 ±0.9	13.5 ±5.1	295.0 ±1.0	292.0 ±4.4	15.8 ±0.4	15.6 ±1.5	51.4 ±0.4	48.9 ±3.3	5.4 ±0.2	5.2 ±0.5‡	-13.5 ±2.3	-13.4 ±5.2

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET), lactate concentration ([La]), osmolality ([OSM]), hemoglobin concentration ([Hb]), hematocrit (Hct), red blood cell concentration ([RBC]).

Table 18. Combined Group Resting and Maximal Metabolic and Hematologic Parameters.

Condition	Time	[La] ($mM \cdot l^{-1}$)	[Osm] (osmol•kg H_2O^{-1})	[Hb] ($g \cdot dl^{-1}$)	Hct (%)	[RBC] ($10^6 \cdot \mu l^{-1}$)	Plasma Volume (% Change from Rest)
SL	Rest	1.7±0.9	287.7±4.7	14.6±1.1	46.8±3.4	5.0±0.3	
	Max	14.5±3.0	293.5±3.9	15.9±1.0	51.3±3.1	5.4±0.3	-16.1±2.5
Pre Ac	Rest	1.9±0.5	283.8±2.6	14.4±0.8	46.2±2.0	4.9±0.2	
	Max	12.7±3.8	291.3±2.4	15.4±0.6*	49.5±1.5*	5.2±0.2*	-12.5±3.0*
Post Ac	Rest	3.3±1.6	286.0±3.9	14.7±1.1†	46.0±3.6	4.9±0.3	
	Max	15.0±3.6	293.5±3.3	15.7±1.0*†	50.1±2.5	5.3±0.3	-13.4±3.6

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc), lactate concentration ([La]), osmolality ([OSM]), hemoglobin concentration ([Hb]), hematocrit (Hct), red blood cell concentration ([RBC]).

Table 19. Group Resting and Maximal Acid-Base Parameters.

Condition	Time	pH		PO_2 (mmHg)		PCO_2 (mmHg)		$[HCO_3^-]$ ($mEq \cdot l^{-1}$)		[BE] ($mEq \cdot l^{-1}$)	
		PS	ET	PS	ET	PS	ET	PS	ET	PS	ET
SL	Rest	7.43 ±0.01	7.42 ±0.01	83.2 ±8.1	81.9 ±5.3	41.2 ±0.1	42.3 ±0.3	27.1 ±0.6	27.1 ±0.4	3.0 ±1.1	2.6 ±0.6
	Max	7.24 ±0.04	7.26 ±0.03	95.1 ±8.3	92.1 ±10.1	30.9 ±4.7	31.7 ±3.2	12.7 ±2.5	13.7 ±2.1	-13.4 ±2.9	-11.6 ±2.7
Pre Ac	Rest	7.47 ±0.02	7.43 ±0.02	41.6 ±4.4*	38.7 ±0.7*	38.2 ±2.3	40.6 ±0.6	27.4 ±0.5	26.6 ±0.6	4.4 ±0.5	3.0 ±0.9
	Max	7.28 ±0.04*	7.31 ±0.03*	55.3 ±3.8*	51.4 ±5.3*	27.9 ±6.8	31.1 ±2.2	12.9 ±4.2	15.3 ±2.3	-12.2 ±4.5	-9.3 ±2.8
Post Ac	Rest	7.47 ±0.03	7.45 ±0.04	46.7 ±5.2*	42.9 ±6.6*	33.5 ±2.2*†	35.4 ±1.9*†	23.5 ±0.3*†	24.1 ±1.2*†	0.2 ±0.8	2.0 ±1.1
	Max	7.23 ±0.02*	7.27 ±0.09	68.0 ±13.9*	55.5 ±2.6*	23.1 ±4.5*†	26.0 ±1.5*†	9.4 ±1.9*†	12.0 ±3.2*†	-15.4 ±2.3	-14.3 ±5.6

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET), partial pressure of arterial oxygen (PO_2), partial pressure of arterial carbon dioxide (PCO_2), bicarbonate concentration ($[HCO_3^-]$, base excess ([BE]).

Table 20. Combined Group Resting and Maximal Acid-Base Parameters.

Condition	Time	pH	PO_2 (mmHg)	PCO_2 (mmHg)	$[HCO_3^-]$ ($mEq \cdot l^{-1}$)	[BE] ($mEq \cdot l^{-1}$)
SL	Rest	7.43 ±0.01	82.5 ±6.2	41.7±0.7	27.1±0.4	2.8±0.8
	Max	7.25 ±0.03	93.6 ±8.4	31.3±3.6	13.2±2.1	-12.5±2.7
Pre Ac	Rest	7.45 ±0.03	40.1 ±3.2*	39.4±2.0	27.0±0.6	3.7±1.1
	Max	7.30 ±0.03*	53.3 ±4.6*	29.5±4.8	14.1±3.3	-10.8±3.7*
Post Ac	Rest	7.46 ±0.03*	44.8 ±5.7*	34.5±2.1*†	23.8±0.8*†	1.1±1.3
	Max	7.25 ±0.06†	61.8 ±11.2*	24.6±3.4*†	10.7±2.7*†	-14.9±3.9

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc), partial pressure of arterial oxygen (PO_2), partial pressure of arterial carbon dioxide (PCO_2), bicarbonate concentration ($[HCO_3^-]$), base excess ([BE]).

Table 21. Group Ventilatory Parameters Measured at Rest and During Submaximal Exercise.

Condition	Time	$\dot{V}O_2$ ($l \cdot min^{-1}$)		$\dot{V}E$ ($l \cdot min^{-1}$)		$\dot{V}E \cdot \dot{V}O_2^{-1}$		$\dot{V}E \cdot \dot{V}CO_2^{-1}$		SaO_2 (%)		RER	
		PS	ET	PS	ET	PS	ET	PS	ET	PS	ET	PS	ET
SL	Rest	0.36 ±0.06	0.37 ±0.11	12 ±1	12 ±2	32.6 ±3.0	32.4 ±3.0	36.0 ±1.2	36.1 ±3.9	99 ±1	99 ±1	0.90 0.05	0.91 0.03
	40%	1.49 ±0.22	1.40 ±0.39	39 ±3	39 ±12	26.5 ±1.8	28.1 ±1.8	27.6 ±1.5	28.7 ±1.3	99 ±1	99 ±1	0.96 0.07	0.98 0.03
	70%	2.48 ±0.63	2.35 ±0.80	75 ±22	79 ±28	30.3 ±1.3	33.6 ±3.2	29.2 ±2.6	33.1 ±3.8	98 ±2	98 ±2	1.04 0.05	1.01 0.02
Pre Ac	Rest	0.39 ±0.03	0.35 ±0.07	17 ±3	14 ±4	43.1 ±3.8*	38.8 ±3.7	50.2 ±1.7*	46.5 ±1.4*	86 ±8*	79 ±2*	0.86 0.09	0.84 0.08
	40%	1.24 ±0.12	1.07 ±0.29*	47 ±6	41 ±12	37.8 ±1.8*	37.9 ±2.0*	41.9 ±3.1*	44.3 ±1.4*	79 ±8*	73 ±5*	0.90 0.03	0.86 0.02*
	70%	2.00 ±0.59*	1.66 ±0.49*‡	92 ±34*	74 ±32‡	45.5 ±3.3*	43.9 ±8.4*	42.6 ±2.2*	46.7 ±6.2*	77 ±5*	71 ±4*	1.06 0.07	0.94 0.05‡
Post Ac	Rest	0.39 ±0.11	0.35 ±0.10	19 ±5	16 ±5	49.9 ±1.3*	44.9 ±4.1*	57.0 ±5.0*	51.9 ±1.6*	90 ±3*	90 ±3*†	0.88 0.07	0.86 0.08
	40%	1.17 ±0.13*	1.01 ±0.28*	47 ±3	42 ±14	39.9 ±1.6*	41.2 ±4.9*	45.1 ±2.3*	46.8 ±3.9*	83 ±4*	84 ±6*†	0.89 0.08	0.88 0.06
	70%	2.04 ±0.60*	1.62 ±0.49*‡	95 ±35*	77 ±24‡	45.7 ±3.2*	47.9 ±4.9*	45.7 ±3.2*	47.8 ±4.9*	79 ±6*	77 ±2*	0.98 0.04	0.92 0.06

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET); 40% of altitude-specific pre-training $\dot{V}O_{2max}$ (40%); 70% of altitude-specific pre-training $\dot{V}O_{2max}$ (70%), Oxygen uptake ($\dot{V}O_2$), Minute ventilation ($\dot{V}E$), Ventilatory equivalent for oxygen ($\dot{V}E \cdot \dot{V}O_2^{-1}$), Ventilatory equivalent for carbon dioxide ($\dot{V}E \cdot \dot{V}CO_2^{-1}$), Arterial oxygen saturation (SaO_2), Respiratory exchange ratio (RER).

Table 22. Combined Group Ventilatory Parameters Measured at Rest and During Submaximal Exercise.

Condition	Time	$\dot{V}O_2$ ($l \cdot min^{-1}$)	$\dot{V}E$ ($l \cdot min^{-1}$)	$\dot{V}E \cdot \dot{V}O_2^{-1}$	$\dot{V}E \cdot \dot{V}CO_2^{-1}$	SaO_2 (%)	RER
SL	Rest	0.36±0.08	12±2	32.5±2.7	36.1±2.6	99±1	0.90±0.04
	40%	1.44±0.28	39±8	27.3±1.8	28.1±1.4	99±1	0.97±0.05
	70%	2.42±0.65	77±22	31.9±2.8	31.2±3.6	98±1	1.02±0.04
Pre Ac	Rest	0.37±0.05	15±3	40.9±4.1*	48.3±2.5*	82±6*	0.85±0.08
	40%	1.16±0.22*	44±9	37.9±1.7*	43.1±2.5*	76±7*	0.88±0.03*
	70%	1.82±0.52*	83±31	44.7±5.8*	44.7±4.7*	74±5*	1.00±0.09
Post Ac	Rest	0.37±0.10	18±5	47.4±3.9*†	54.4±4.4*†	90±2*†	0.87±0.07
	40%	1.09±0.21*	44±9	40.5±3.3*	46.0±3.0*	84±5*†	0.88±0.06*
	70%	1.83±0.54*	86±29	46.8±3.9*	46.8±3.9*	78±4*	0.95±0.06*

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); 40% of altitude-specific pre-training $\dot{V}O_{2max}$ (40%); 70% of altitude-specific pre-training $\dot{V}O_{2max}$ (70%), Oxygen uptake ($\dot{V}O_2$), Minute ventilation ($\dot{V}E$), Ventilatory equivalent for oxygen ($\dot{V}E \cdot \dot{V}O_2^{-1}$), Ventilatory equivalent for carbon dioxide ($\dot{V}E \cdot \dot{V}CO_2^{-1}$), Arterial oxygen saturation (SaO_2), Respiratory exchange ratio (RER).

Table 23. Group Cardiovascular Parameters Measured at Rest and During Submaximal Exercise.

Condition	Time	HR (beats•min^{-1})		MAP (mmHg)		O_2 Pulse (ml•beat^{-1})		CaO_2 (ml O_2•l^{-1})	
		PS	ET	PS	ET	PS	ET	PS	ET
SL	Rest	66±12	78±15	83±2	81±11	5.1±1.3	4.2±0.6	192±2	189±17
	40%	112±12	121±10	87±1	89±2	12.9±2.4	11.3±3.5	200±8	200±16
	70%	159±5	167±9	93±2	99±12	16.0±3.1	14.3±5.0	207±8	204±14
	EX	182±8	186±6	93±6	96±8			209±8	204±16
PreAc	Rest	79±2	108±12*‡	90±7	84±5	4.3±0.9	2.8±1.0	178±13	159±16*
	40%	122±16	140±20*‡	93±3	92±2	9.3±2.0*	6.8±2.5*	169±16*	156±25*
	70%	152±16	165±17	93±1	95±6	14.2±4.4	9.7±4.0*‡	169±16*	154±17*
	EX	159±18*	160±15*	91±5	94±4			162±6*	161±15*
PostAc	Rest	72±2	86±19†	94±8	89±7	4.8±1.5	3.8±1.9	185±5	180±32†
	40%	109±10	119±20†	94±11	96±10	9.5±1.0*	7.8±3.0*	175±9*	176±31*†
	70%	142±14*	148±22*†	98±13	100±7	14.0±8.6	10.6±4.2*‡	171±14*	164±21*
	EX	157±10*	166±14*	94±2	96±4			175±5*	173±10*

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET); 40% of altitude-specific pre-training VO_{2max} (40%); 70% of altitude-specific pre-training VO_{2max} (70%); exhaustion (EX), Heart rate (HR), Mean Arterial Pressure (MAP), Arterial oxygen content (CaO_2).

Table 24. Combined Group Cardiovascular Parameters Measured at Rest and During Submaximal Exercise.

Condition	Time	HR (beats•min^{-1})	MAP (mmHg)	O_2 Pulse (ml•beat^{-1})	CaO_2 (ml O_2•l^{-1})
SL	Rest	72±14	82±7	4.6±1.0	191±11
	40%	116±11	88±2	12.1±2.8	200±11
	70%	163±8	96±8	15.2±3.8	206±10
	EX	184±7	95±7		207±12
Pre Ac	Rest	93±18	87±6	3.6±1.2	168±17*
	40%	131±19	92±2	8.1±2.5	163±20*
	70%	158±17	94±4	12.0±4.5	161±17*
	EX	160±15	93±4		161±11*
Post Ac	Rest	78±14	92±7	4.3±1.6	182±21†
	40%	114±15	95±9	8.7±2.2	175±21*†
	70%	145±17	99±9	12.3±3.8	168±16*
	EX	162±12	95±3		174±9*†

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); 40% of altitude-specific pre-training VO_{2max} (40%); 70% of altitude-specific pre-training VO_{2max} (70%); exhaustion (EX), Heart rate (HR), Mean Arterial Pressure (MAP), Arterial oxygen content (CaO_2).

Table 25. Group Hematologic Parameters Measured at Rest and During Submaximal Exercise.

Condition	Time	[EPO] ($mU \cdot ml^{-1}$)		[Hb] ($g \cdot dl^{-1}$)		Hct (%)		[RBC] ($10^6 \cdot \mu l^{-1}$)		Plasma Volume (% Change from Rest)	
		PS	ET	PS	ET	PS	ET	PS	ET	PS	ET
SL	Rest	8±2	10±2	14.3±0.3	14.0±1.2	47.0±0.5	44.0±3.4‡	4.9±0.1	4.6±0.3		
	40%	9±3	11±2	14.8±0.7	14.9±1.3	49.0±2.1	46.1±2.6‡	5.1±0.1	5.0±0.3	-7.2±5.9	-9.5±2.0
	70%	8±2	11±3	15.5±0.7	15.4±1.2	50.1±1.5	46.8±1.8‡	5.4±0.2	5.2±0.3	-13.4±3.4	-13.6±4.3
	EX	8±3	11±2	15.6±0.7	15.6±1.3	50.4±1.1	47.5±3.4‡	5.2±0.2	5.2±0.4	-14.4±3.2	-15.7±4.5
PreAc	Rest	60±25*	124±40*‡	15.3±0.6	14.7±1.2	49.1±1.7	45.5±3.3‡	5.2±0.1	4.9±0.4		
	40%	63±28*	131±53*‡	15.8±1.1	15.6±1.6	49.9±2.0	47.8±3.2	5.4±0.2	5.2±0.5	-4.5±4.5	-9.5±1.2
	70%	67±34*	127±44*‡	16.1±0.9	16.0±1.4	50.6±1.8	48.5±2.7	5.5±0.2	5.4±0.4	-7.8±2.6	-13.3±3.0
	EX	62±30*	136±48*‡	16.4±0.3	15.7±1.3	51.2±1.6	48.0±2.8‡	5.4±0.2	5.2±0.4	-10.4±4.1	-10.7±2.5
PostAc	Rest	40±14*†	69±26*†‡	15.1±0.3	14.6±2.2	47.7±1.7	45.7±5.2	5.2±0.1	4.9±0.6		
	40%	41±15*†	71±29*†‡	15.6±0.2	15.2±1.8	49.5±0.5	47.1±4.3	5.3±0.2	5.1±0.4	-6.1±2.9	-6.6±4.9
	70%	40±14*†	72±29*†‡	16.0±0.3	15.6±1.6	50.6±0.4	47.4±3.8‡	5.4±0.1	5.2±0.6	-10.5±2.7	-9.1±7.2
	EX	38±14*†	71±31*†‡	16.3±0.4	15.9±1.6	50.8±0.4	49.1±2.9	5.6±0.1	5.3±0.4	-12.7±1.5	-13.6±9.3

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET); 40% of altitude-specific pre-training VO_{2max} (40%); 70% of of altitude-specific pre-training VO_{2max} (70%); exhaustion (EX), Erythropoietin concentration ([EPO]), Hemoglobin concentration ([Hb]), Hematocrit (Hct), Red blood cell concentration ([RBC]).

Table 26. Combined Group Hematologic Parameters Measured at Rest and During Submaximal Exercise.

Condition	Time	$[EPO]^{-1}$ ($mU \cdot ml^{-1}$)	[Hb] ($g \cdot dl^{-1}$)	Hct (%)	RBC ($10^6 \cdot \mu l^{-1}$)	Plasma Volume (% Change from Rest)
SL	Rest	9±2	14.1±0.8	45.5±2.7	4.8±0.3	
	40%	10±3	14.8±0.9	47.5±2.6	5.0±0.2	-8.3±4.2
	70%	10±3	15.4±0.9	48.5±2.3	5.3±0.2	-13.5±3.5
	EX	10±3	15.6±1.0	48.9±2.7	5.2±0.3*	-15.1±2.4
Pre Ac	Rest	92±46*	15.0±0.9*	47.3±3.1*	5.1±0.3	
	40%	97±53*	15.7±1.3*	48.9±2.6	5.3±0.3	-7.0±4.5
	70%	97±49*	16.1±1.1*	49.6±2.4	5.5±0.3	-10.5±3.4
	EX	99±54*	16.1±1.0	49.6±2.7	5.3±0.3*	-10.6±2.9*
Post Ac	Rest	54±25*†	14.9±1.4*	46.7±3.7	5.0±0.4	
	40%	56±26*†	15.4±1.1*	48.3±3.1	5.2±0.3	-6.3±3.6
	70%	56±27*†	15.8±1.1	49.0±3.0	5.3±0.4	-9.8±4.9
	EX	54±28*†	16.1±1.1	50.0±2.1	5.4±0.3	-13.1±6.0

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); 40% of altitude-specific pre-training VO_{2max} (40%); 70% of altitude-specific pre-training VO_{2max} (70%); exhaustion (EX), Erythropoietin concentration ([EPO]), Hemoglobin concentration ([Hb]), Hematocrit (Hct), Red blood cell concentration ([RBC]).

Table 27. Group Metabolic and Hormonal Parameters Measured at Rest and During Submaximal Exercise.

Condition	Time	[La] ($mM \cdot l^{-1}$)		[EPI] ($pg \cdot ml^{-1}$)		[NOR] ($pg \cdot ml^{-1}$)		[COR] ($\mu g \cdot dl^{-1}$)	
		PS	ET	PS	ET	PS	ET	PS	ET
SL	Rest	1.7±0.7	1.7±0.5	48±27	30±10	543±108	322±124	17.1 ±5.4	8.2±3.2
	40%	2.7±1.3	2.3±0.1	119±119	54±7	512±182	536±144	15.6±2.2	6.4±3.6
	70%	8.9±2.4	8.1±1.9	198±99	182±75	1625±422	1911±656	14.8±3.9	6.6±3.5
	EX	12.3±3.9	11.3±4.1	445±91	385±200	2894±568	3292±1072	15.0±3.1	12.4±6.2
PreAC	Rest	1.8±0.4	2.2±0.9	39±7	49±5	461±13	469±116	13.2±2.4	11.6±3.1
	40%	2.8±1.1	2.6±0.7	52±25	79±12	681±161	625±54	10.4±1.7	13.4±4.1
	70%	7.7±0.9	6.4±1.4	100±41	179±67	1696±573	1723±630	9.7±2.2	14.1±3.9*
	EX	11.1±2.2	6.5±2.7*‡	234±44*	274±130*	3282±1702	2273±790	19.5±3.0	19.7±6.6
PostAc	Rest	1.6±0.7	1.7±0.5	40±31	114±141	613±223	598±195	12.9±2.0	10.6±5.0
	40%	2.3±0.8	1.9±0.5	45±13	114±131	781±268	658±165	10.8±2.3	10.5±3.4
	70%	5.5±1.3*	3.7±1.1*	93±36	148±109	1758±1359	1084±261	12.7±1.0	11.1±4.4
	EX	9.8±0.8	9.0±2.8	236±101*	339±136	3595±1391	3250±1911	20.2±1.1	14.8±5.6

Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); Passive Sitting (PS); Exercise-Training (ET); 40% of altitude-specific pre-training VO_{2max} (40%); 70% of altitude-specific pre-training VO_{2max} (70%); exhaustion (EX), Lactate concentration ([La]), Epinephrine concentration ([EPI]), Norepinephrine concentration ([NOR]), Cortisol concentration ([COR]).

Table 28. Combined Group Metabolic and Hormonal Parameters Measured at Rest and During Submaximal Exercise.

Condition	Time	[La] ($mM \cdot l^{-1}$)	[EPI] ($pg \cdot ml^{-1}$)	[NOR] ($pg \cdot ml^{-1}$)	[COR] ($\mu g \cdot dl^{-1}$)
SL	Rest	1.7±0.5	39±21	432±159	12.6±6.3
	40%	2.5±0.8	87±83	524±148	10.9±5.7
	70%	8.5±2.0	190±79	1768±517	10.7±5.6
	EX	11.8±3.6	415±143	3093±798	13.7±4.6
Pre Ac	Rest	2.0±0.6	44±8	465±73	12.4±2.7
	40%	2.7±0.8	65±23	653±119	11.9±3.3
	70%	7.1±1.3	139±66	1709±539	11.9±3.7
	EX	8.8±3.3*	254±90*	2778±1309	19.6±4.6*
Post Ac	Rest	1.7±0.5	77±100	606±188	11.7±3.7
	40%	2.1±0.6	80±92	720±210	10.7±2.6
	70%	4.6±1.4*†	121±79*	1421±950	11.9±3.0
	EX	9.4±1.9*	288±121*	3423±1507	17.5±4.7*

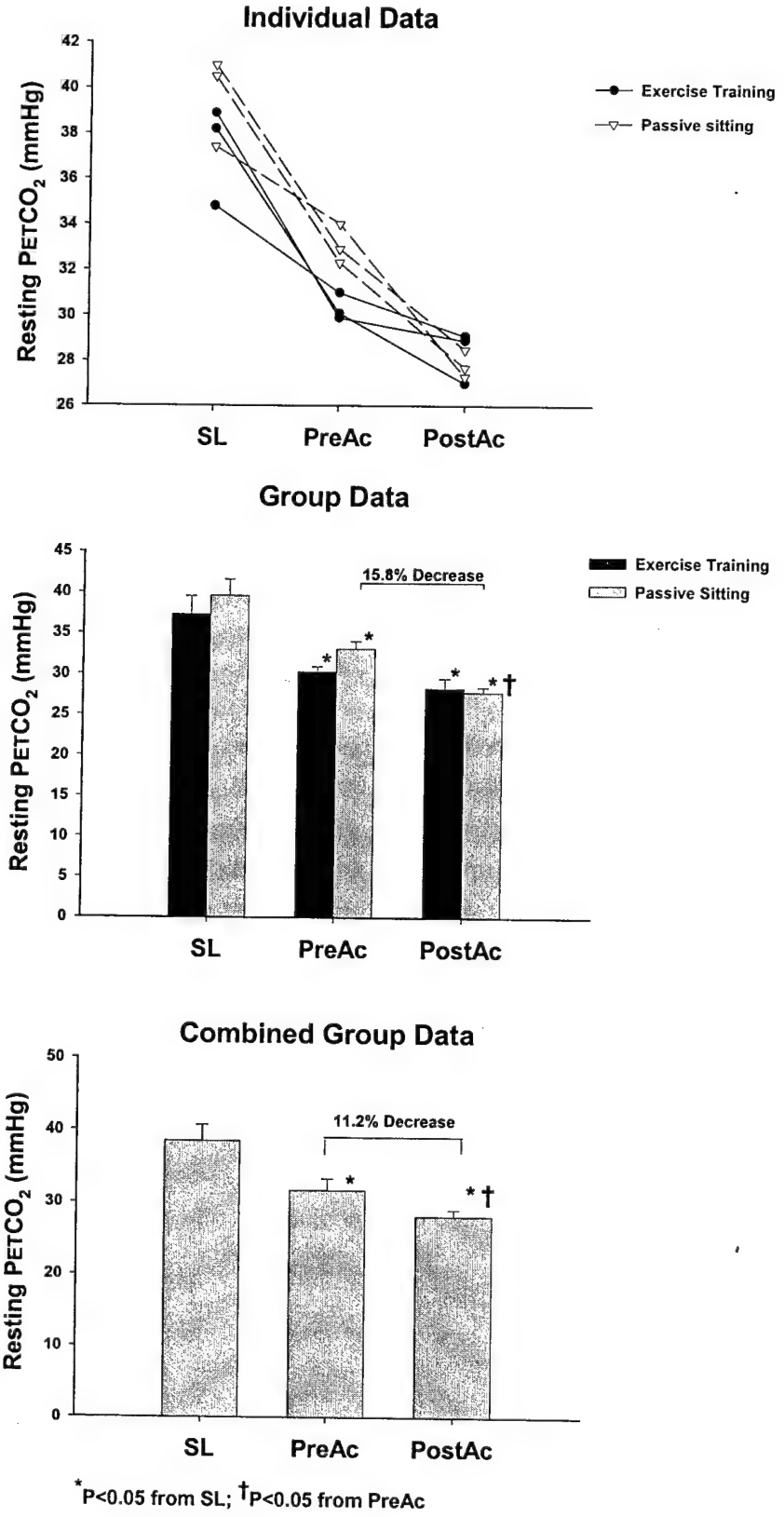
Mean±SD; *P<0.05 from SL; †P<0.05 from PreAc; Sea Level (SL); Pre-Acclimatization (PreAc); Post-Acclimatization (PostAc); 40% of altitude-specific pre-training VO_{2max} (40%); 70% of altitude-specific pre-training VO_{2max} (70%); exhaustion (EX), Lactate concentration ([La]), Epinephrine concentration ([EPI]), Norepinephrine concentration ([NOR]), Cortisol concentration ([COR]).

Table 29. Comparison of the Change in Small-Muscle Endurance Performance (END_{sm}) from PreAc to PostAc with the Results Observed upon Acute Altitude (AA) and Chronic Altitude (CA) Exposure Compared to Sea Level (SL) in Three Chronic Altitude Residence Studies.

Study	Altitude (m)	Days	Hours	SL END_{sm} (min)	AA END_{sm} (min)	CA END_{sm} (min)	% Change (SL-AA)	% Change (AA-CA)	% Regain (AA-CA)/(AA-SL)*100
(27)	4,300	13	312	7.4	5.1	6.6	-31.1	+29.4	65.2
(30)*	4,350	10	240	17.1	14.6	20.2	-14.6	+38.4	224.0
(28)	4,300	20	480	8.3	5.6	7.4	-32.5	+32.1	66.7
Mean (Chronic Studies)	**4,300**	**14**	**288**	**10.9**	**8.4**	**11.4**	**-26.1**	**+33.3**	**118.6**
Mean (This Study)			**60**	**13.4**	**9.2**	**15.0**	**-31.3**	**+64.5**	**138.1**
% of Chronic Response			**20.8**	**N/A**	**N/A**	**N/A**	**N/A**	**193.7**	**116.4**

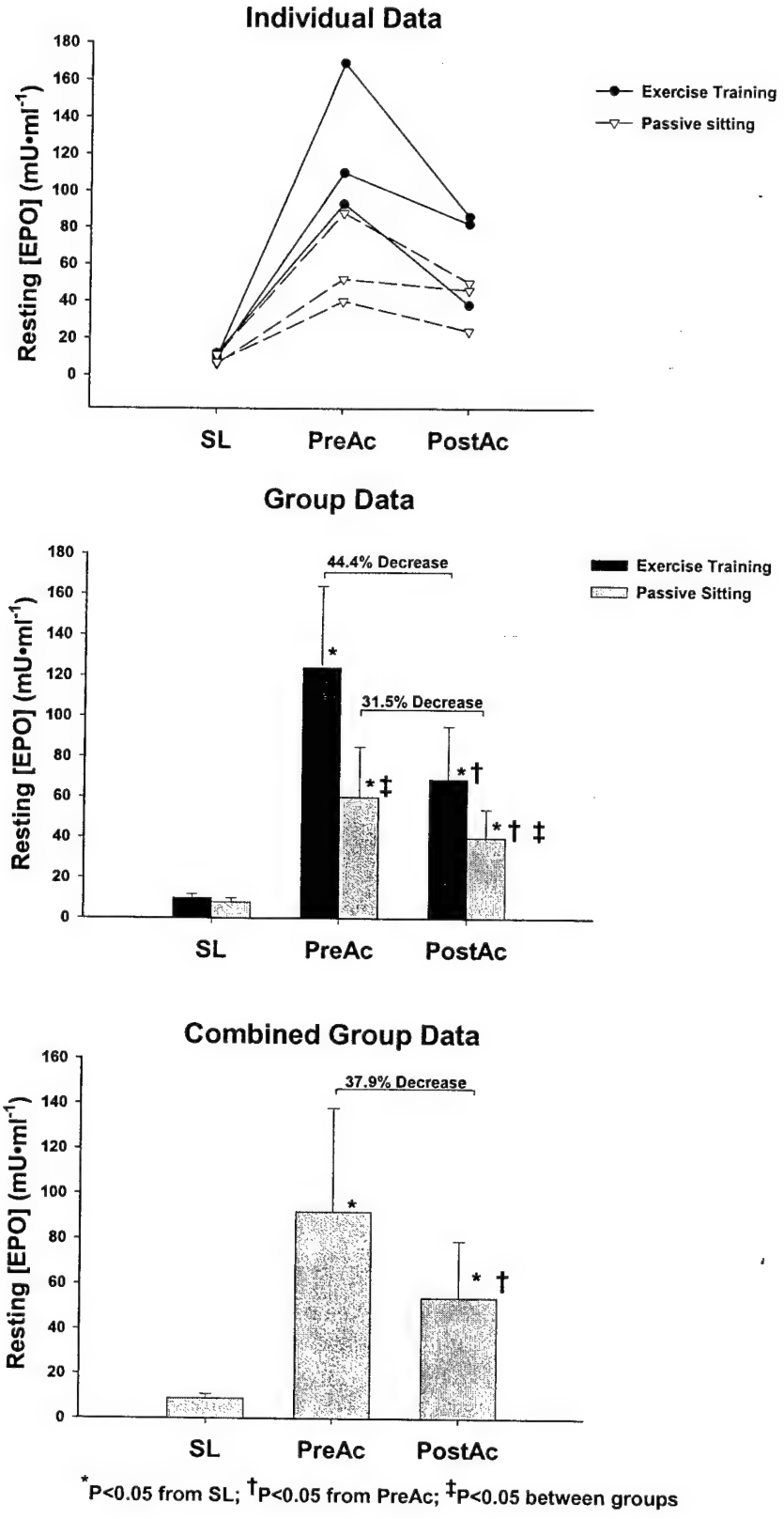
*Denotes females as test volunteers, % Chronic Response (Mean This Study/Mean Chronic Studies)

Figure 2. Resting end-tidal CO_2 ($P_{ET}CO_2$)



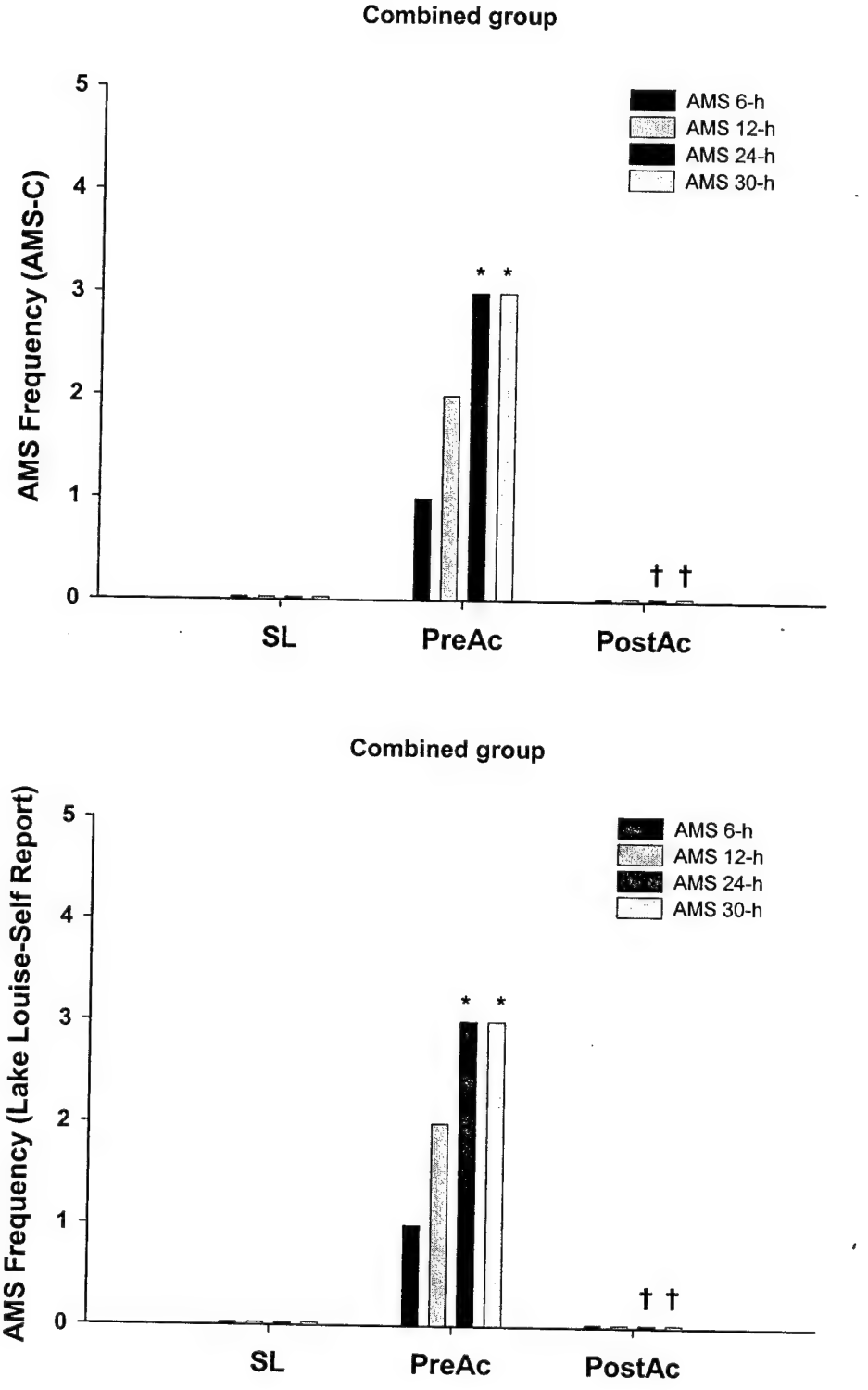
*P<0.05 from SL; †P<0.05 from PreAc

Figure 3. Resting erythropoietin concentration [EPO]



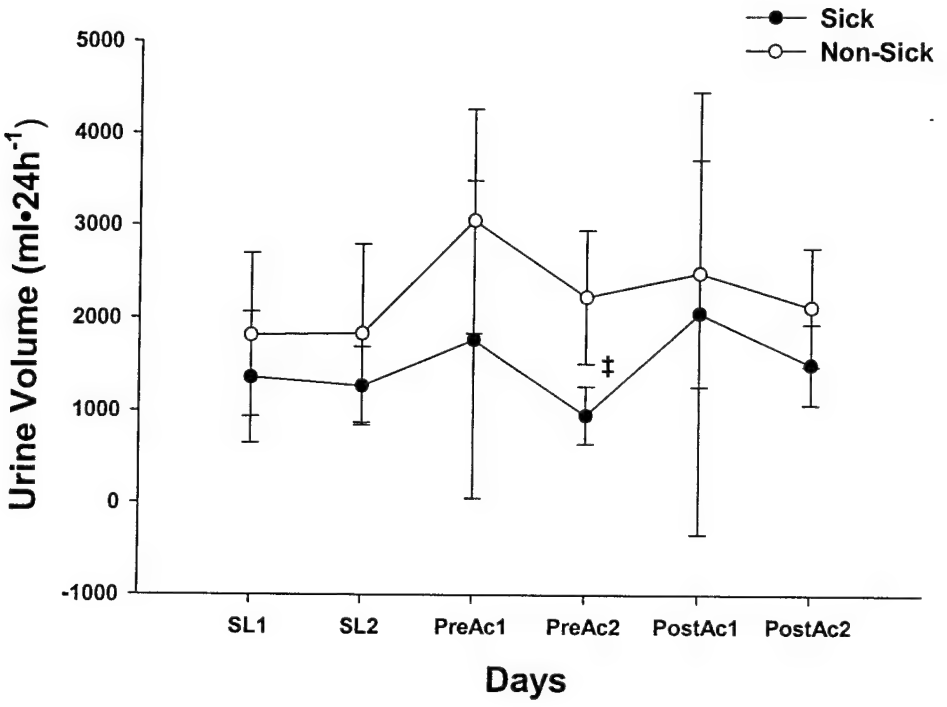
*P<0.05 from SL; †P<0.05 from PreAc; ‡P<0.05 between groups

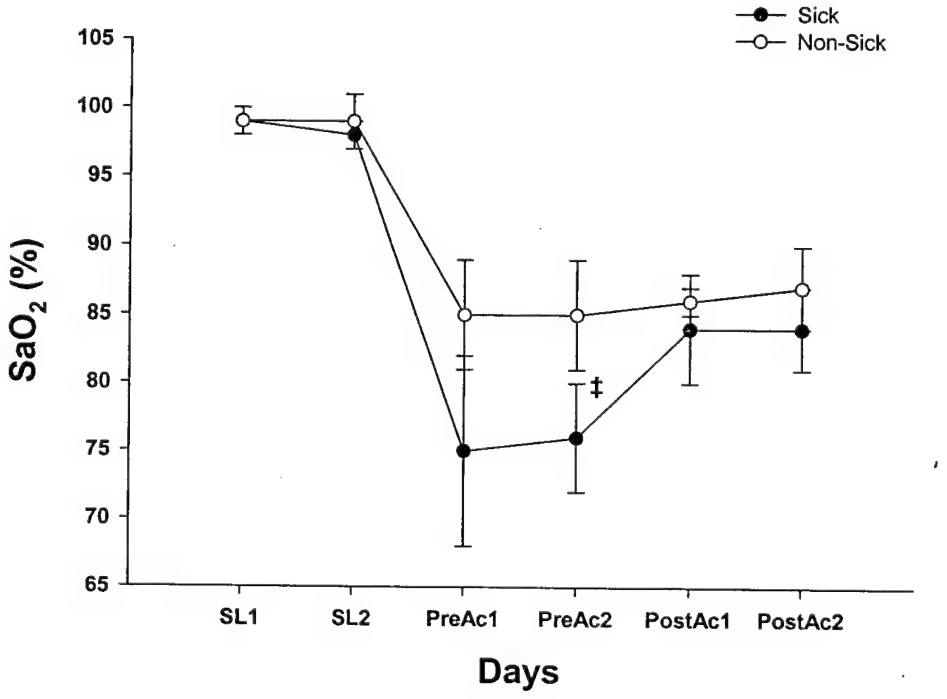
Figure 4. Acute mountain sickness (AMS) frequency scores



*P<0.05 from SL; †P<0.05 from PreAc

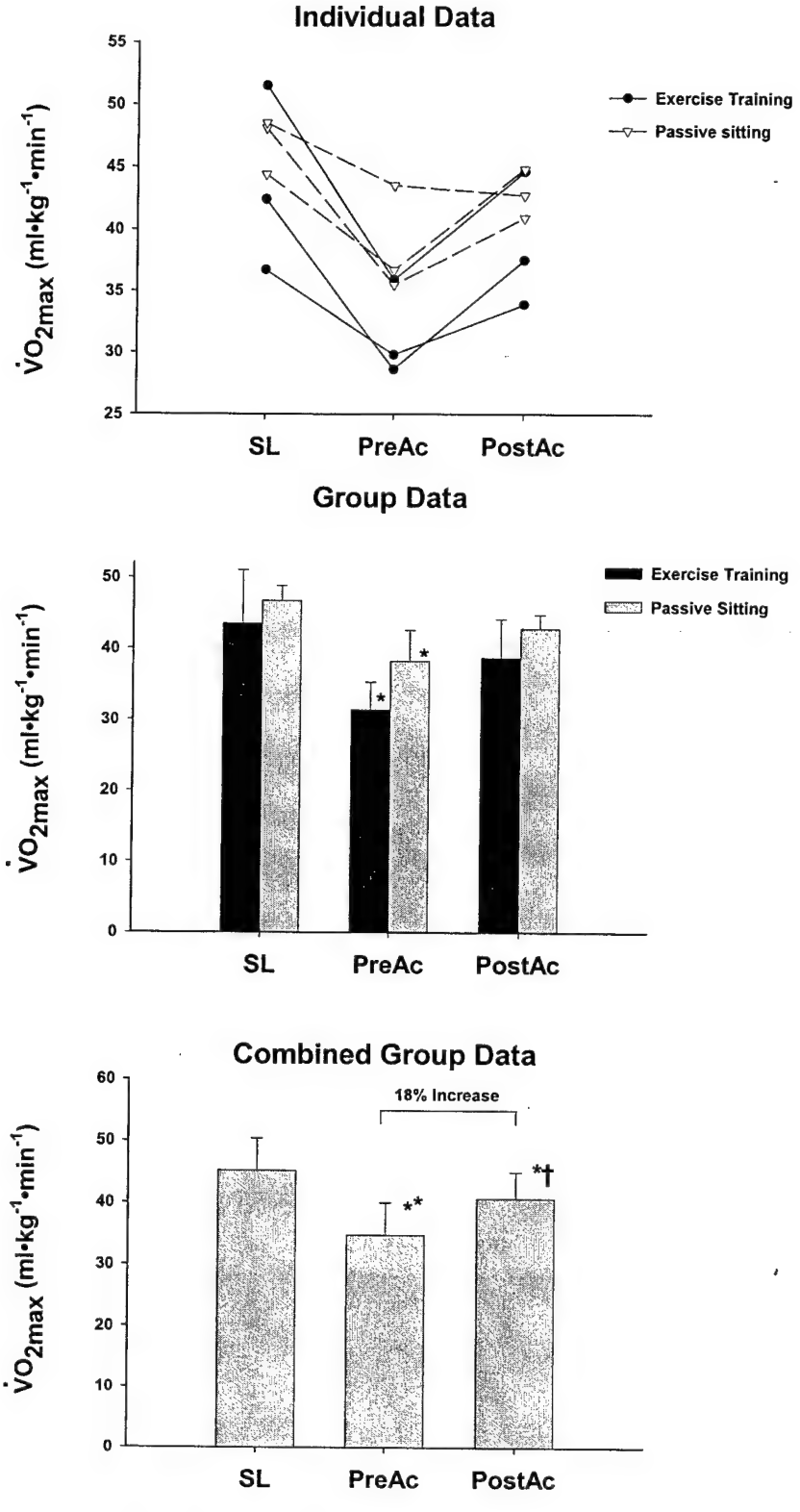
Figure 5. Twenty-four hour urine volume and arterial oxygen saturation (SaO_2) for sick versus non-sick volunteers





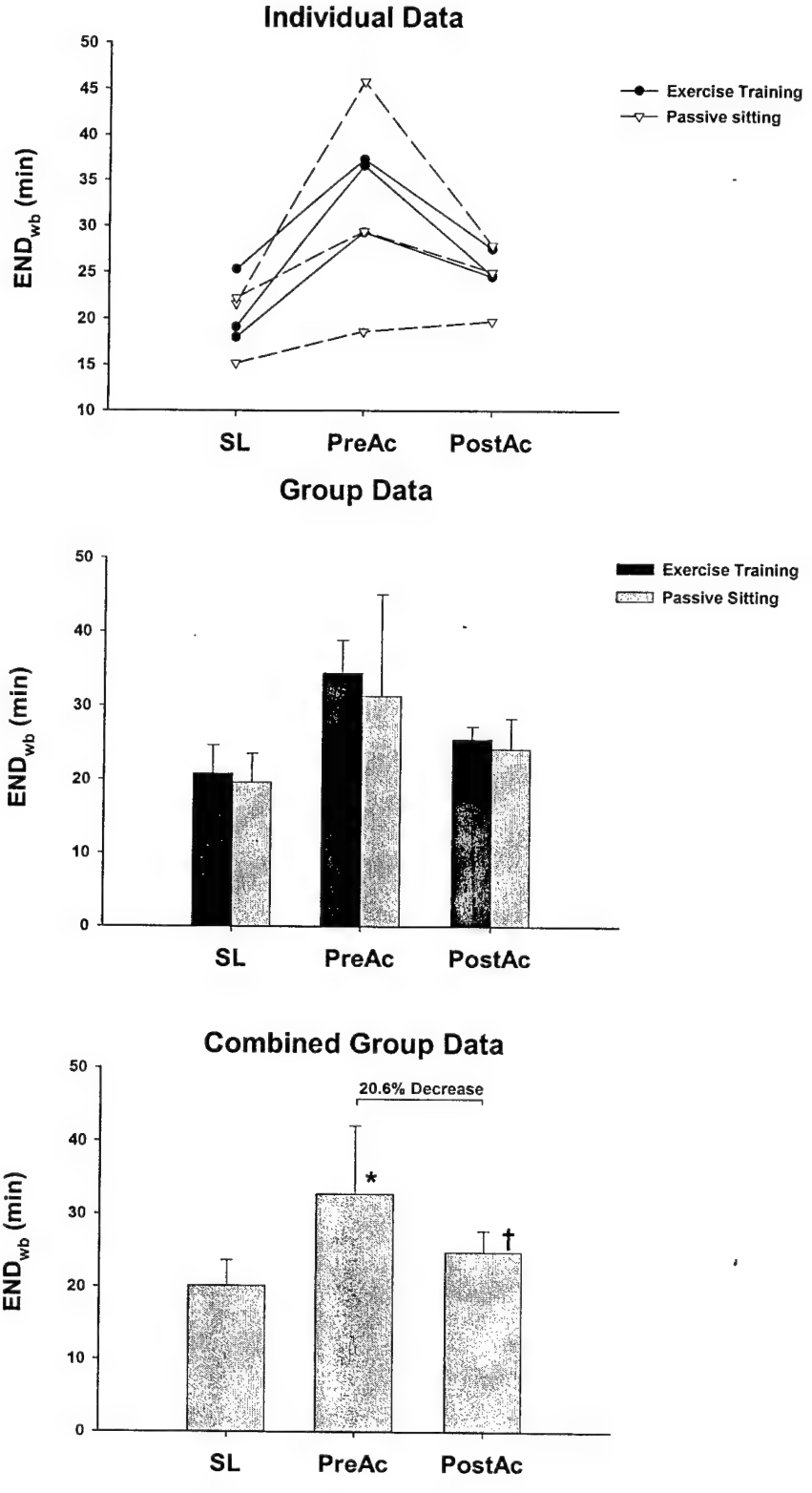
‡ P<0.05 between Sick and Non-Sick volunteers

Figure 6. Maximal oxygen uptake (VO_{2max})



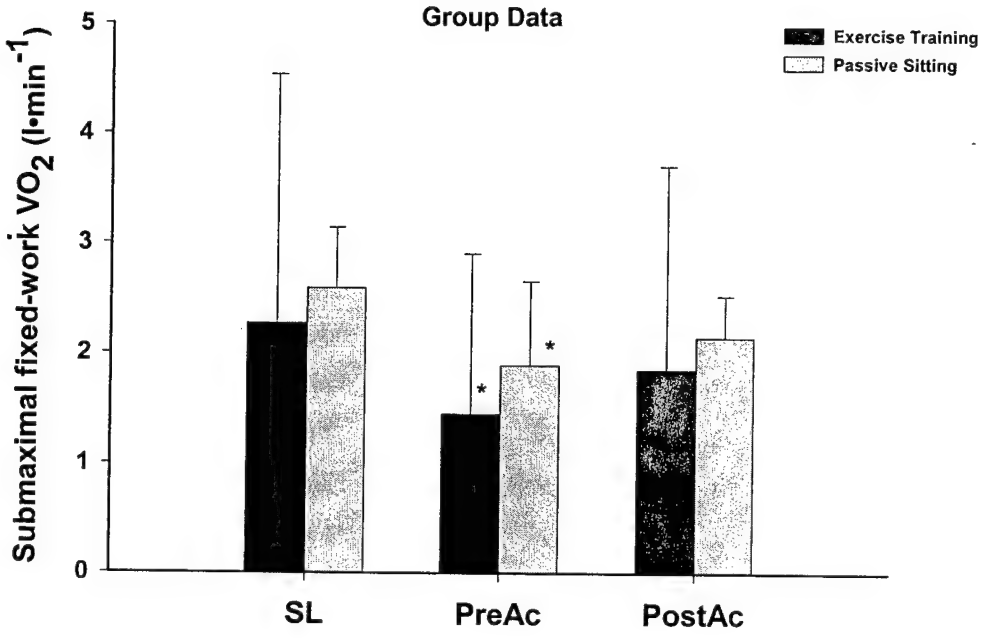
*P<0.05 from SL; †P<0.05 from PreAc

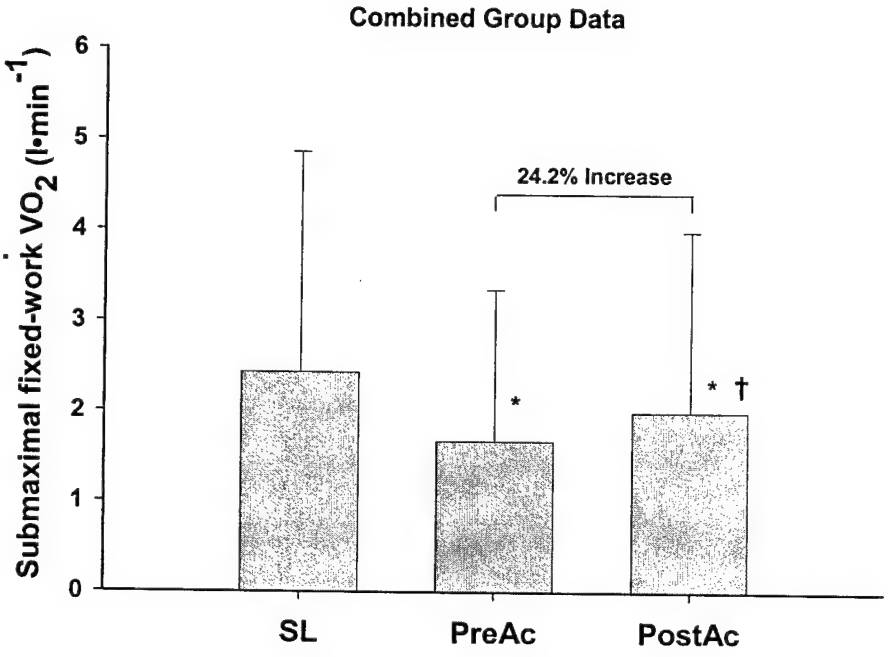
Figure 7. Submaximal whole-body endurance performance (END_{wb})



*P<0.05 from SL; †P<0.05 from PreAc

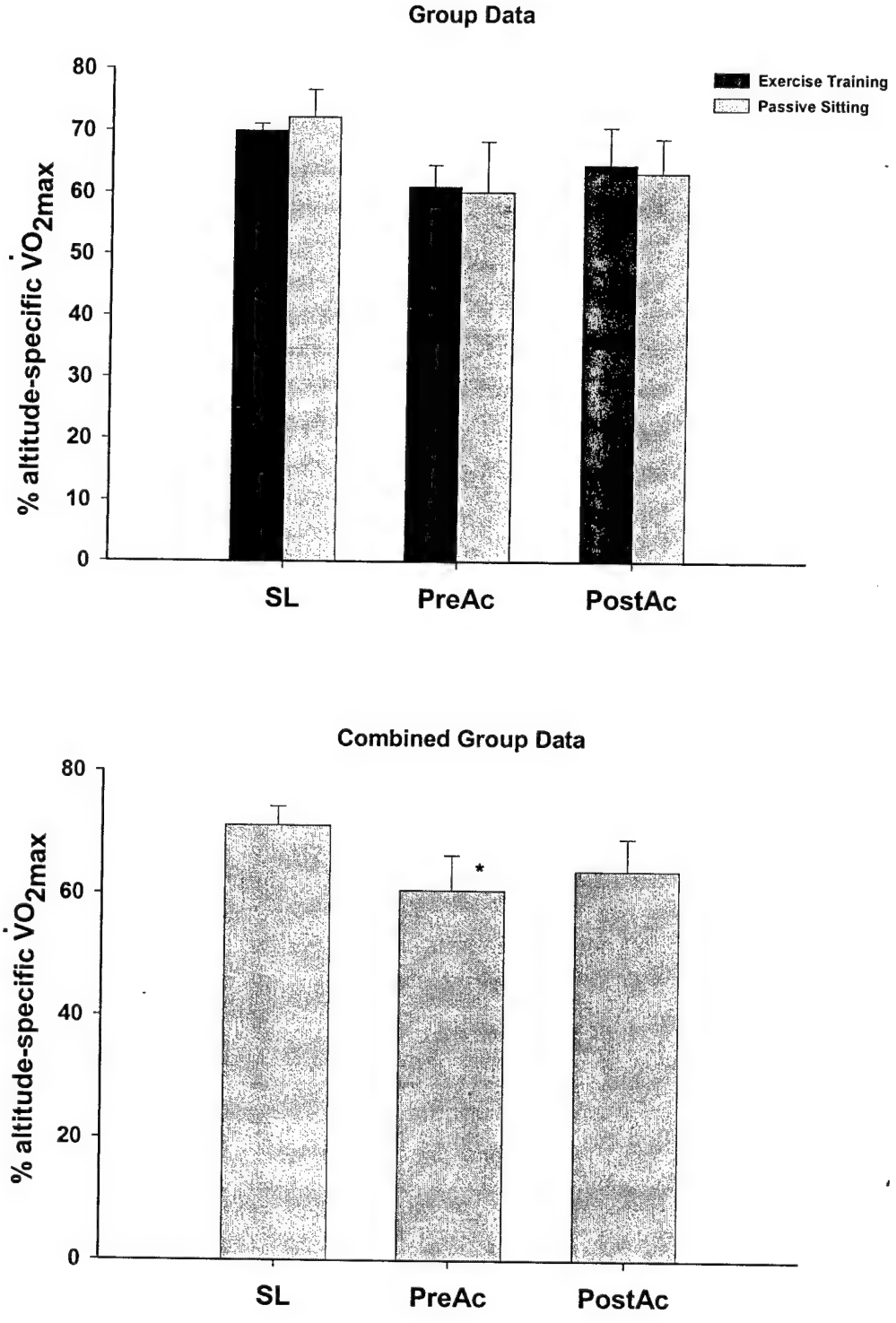
Figure 8. Submaximal fixed-work VO_2





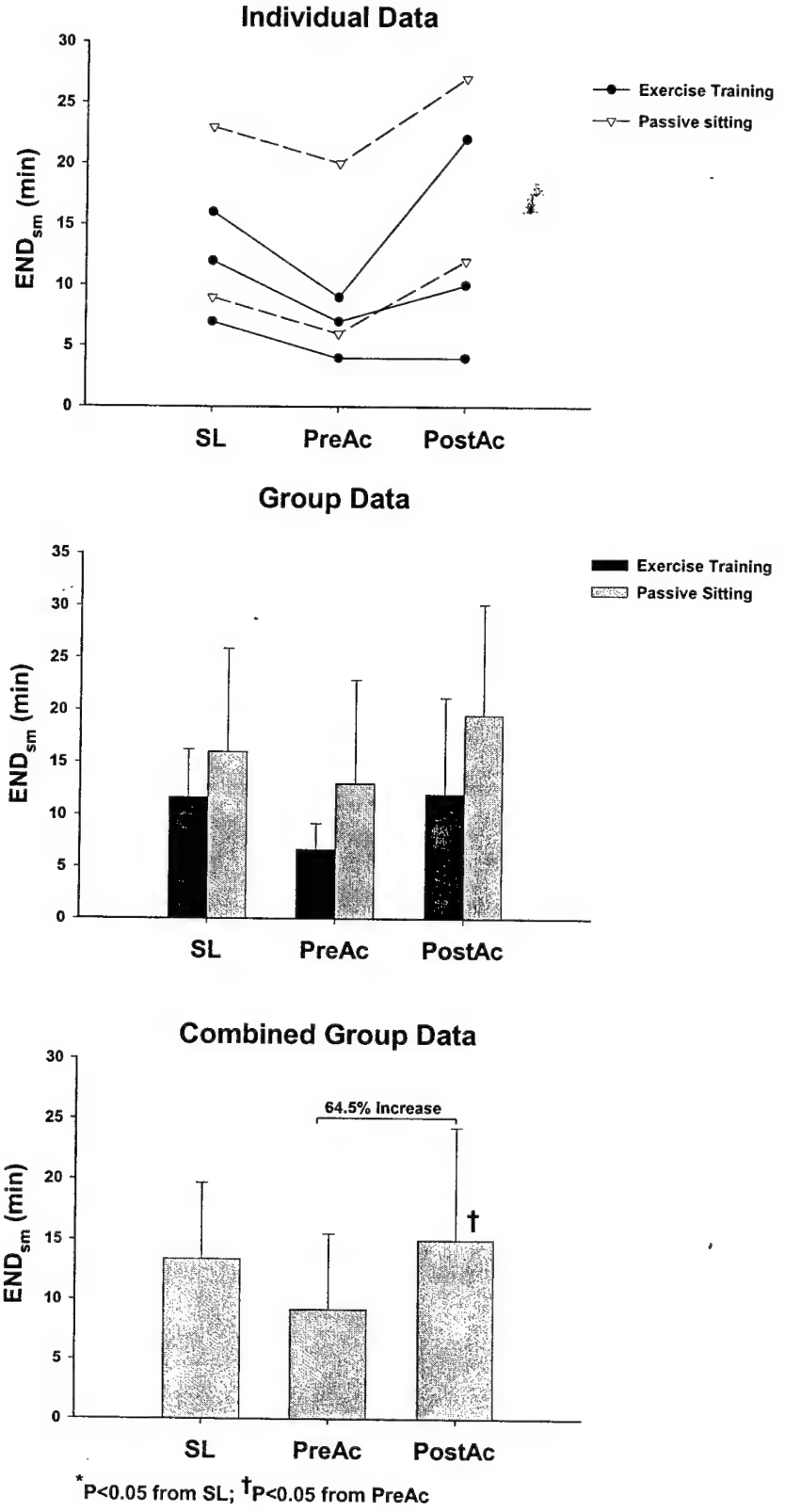
*P<0.05 from SL; †P<0.05 from PreAc

Figure 9. Percentage of altitude-specific $\dot{V}O_{2max}$



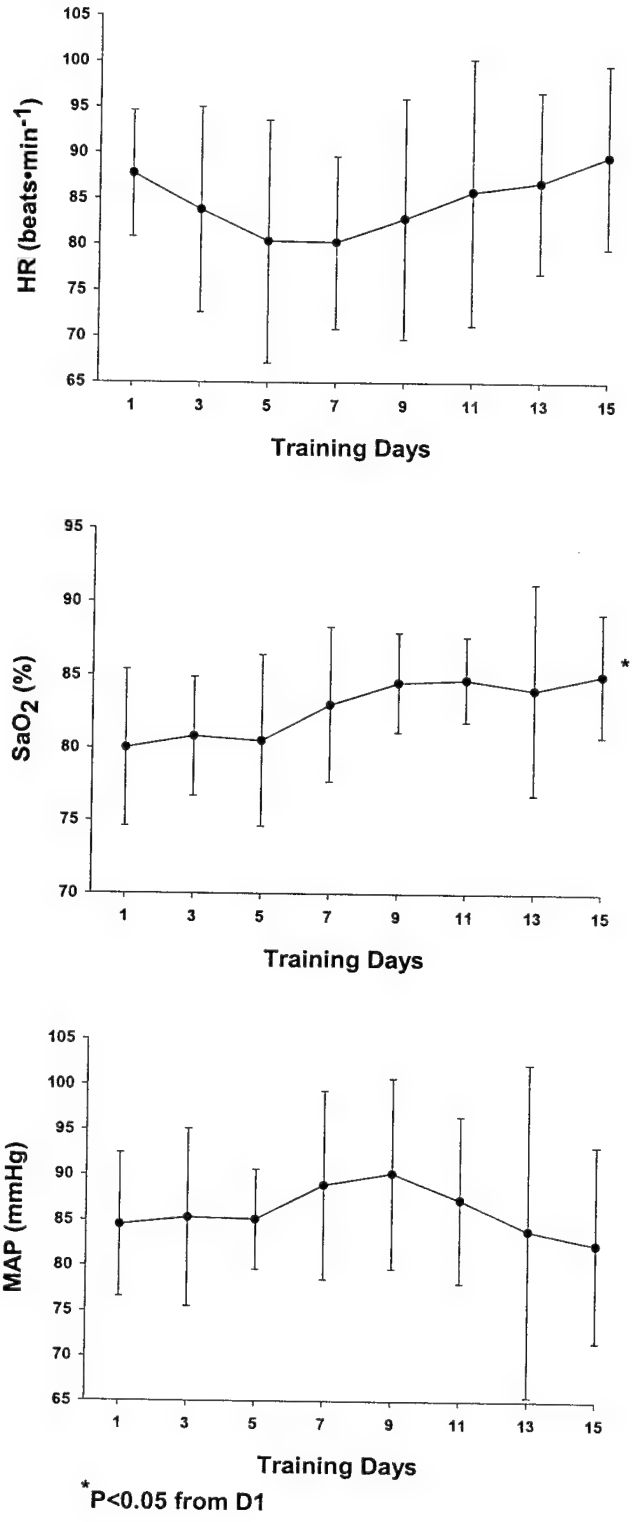
*P<0.05 from SL; †P<0.05 from PreAc

Figure 10. Small muscle endurance performance (END_{sm})



*P<0.05 from SL; †P<0.05 from PreAc

Figure 11. Combined group resting heart rate (HR), arterial oxygen saturation (SaO_2), and mean arterial pressure (MAP) during intermittent altitude exposures



*P<0.05 from D1

DISCUSSION

This study tested the hypothesis that both passive sitting and exercise training during intermittent exposures to 4,300 m altitude would partially acclimatize an individual to 4,300 m altitude. We found that 3 wk of intermittent (i.e., $4h \cdot d^{-1}$; $5d \cdot wk^{-1}$) exposures to 4,300 m accomplished 50%-100% of the expected adaptation to altitude, based on improvements in submaximal endurance performance and absence of altitude illness, when compared to previous studies where individuals resided at 4,300 m for 3 wk. We further hypothesized that exercise training during intermittent exposures to 4,300 m altitude would have a greater effect on acclimatizing an individual to 4,300 m altitude. We found no differences between the passive sitting and exercise training groups in any of the variables measured except for resting [EPO].

Given the lack of between group differences in most of the variables measured, this discussion will focus on acclimatization effects observed for all subjects combined except where insight on exercise training effects may help explain some of our results. One of the limitations of this study is the small subject numbers (n=3) in each group. Thus, the conclusion of no between group differences should be interpreted cautiously given the inherent lack of statistical power when subject numbers are low. However, two other studies have also reported no group differences when comparing passive exposure and low-intensity exercise during intermittent exposures to altitude (49,86). All altitude acclimatization effects observed in those studies were attributed to hypoxia alone, but the exercise training intensities used were much lower than in our study.

A large increase in resting ventilation is one of the key physiological adaptations that must occur in order to successfully acclimatize to altitude. Three weeks of intermittent altitude exposure resulted in 50%-100% of the expected adaptation in ventilation that occurs following chronic altitude residence. However, this adaptation was accomplished in fewer hours, and thus could be considered a more efficient method of acclimatizing people to altitude. Our results support most of the previous research measuring resting ventilation before and after intermittent exposures to various altitudes (49,51,72,88,92), but differ from a recently published study (80). However, that study (80) only exposed volunteers to altitude for $2\ h \cdot d^{-1}$, and a longer exposure time may be needed to induce the beneficial ventilatory changes we observed.

Another well-known physiological adaptation that occurs following chronic altitude residence is the increase in [Hb] of the blood (76,95). Upon acute altitude exposure (i.e., 1-4 d), the increase in [Hb] is due to a decrease in PV (95). With chronic exposure to altitude (i.e., 11-21 d), PV decreases 15%-25% of baseline SL values while [Hb] increases 15% to 25% of baseline SL values (Table 8). The percentage of decrease in PV is remarkably similar to the percentage of increase in [Hb]. This finding suggests that even after 3 wks of altitude residence the increase in [Hb] is due to a decrease in PV and not due to an increase in red blood cell mass. In this study, the percentages of change in [Hb] and PV at PreAc (i.e., 24-h post) were similar to percentages reported following acute altitude exposure (i.e., 1-4 d) in previous chronic altitude studies (Table 8). However, we observed no changes in PV or [Hb] following 3-wk of intermittent altitude exposures. Thus, intermittent altitude exposures did not elicit the same adaptations in [Hb] and PV that occur with chronic altitude residence. The percentage of hematological adaptation achieved for both [Hb] and PV was ~35% of that achieved following chronic altitude residence. This finding agrees with other research comparing hematological acclimatization following intermittent versus chronic altitude exposure (33).

The release of [EPO] upon initial altitude exposure, which stimulates the bone marrow to produce red blood cells, is typically abated following chronic altitude residence (1,65,96). In our study, [EPO] remained elevated approximately 6-fold above SL values. This continual elevation in [EPO] at PostAc is likely due to the repeated triggering effect of the intermittent hypoxic stimuli. Recent research suggests that intermittent hypoxia is more potent in activating hypoxia-inducible factor-1 transcription than sustained hypoxia (75). Given that the EPO gene is turned on by hypoxia-inducible-factor-1 (15,108), this may account for the different [EPO] responses elicited by intermittent and chronic altitude exposure. Intermittent altitude exposures may provide a greater stimulus for increasing RBC mass compared to chronic altitude residence. Although [Hb] and Hct are increased to a much greater degree following chronic altitude residence compared to intermittent altitude exposure (33), these effects are primarily due to the decrease in PV and not expansion of RBC volume (95). If RBC volume can be increased apart from a decrease in PV, then total blood volume could be increased and potentially enhance endurance performance following intermittent altitude exposures. However, given the unchanged [RBC] in this study, it appears that more than 15 d of intermittent altitude exposures are needed to induce this effect.

Our results differ from some but not others that have studied hematological adaptations following intermittent altitude exposures. Most have reported no changes in either [Hb], Hct, and [RBC] following intermittent altitude exposures that involved no sleep at altitude (24,25,70,72,80,88,104), whereas others (all from the same lab) have reported large increases in one or all of these parameters (19,86,87). The higher [Hb] and Hct reported in those studies (19,86,87) may be possible if there was also a large decrease in PV. However, they did not measure or calculate changes in PV. They contend that no change in osmolality is equivalent to no change in PV (87) but this conclusion may be erroneous given that hemoconcentration at altitude, due to PV loss, is typically oncotically-mediated with no change in [Osm] (94). We also found no change in [Osm] but a fairly large (~9%) decrease in PV within 24 h of altitude exposure that was maintained throughout the 3-wk study. Although the large initial and maintained increase in [EPO] following intermittent altitude exposure should provide a stimulus for erythrocyte volume expansion, our similar [RBC] from PreAc to PostAc may not support this conclusion. Savourey et al. (92) and Koistinen et al. (55), in concert with our study, also reported increased resting [EPO] after intermittent altitude exposures with no corresponding increase in [Hb], Hct, or [RBC]. Since we did not measure actual erythrocyte volume or reticulocyte count, we cannot conclude that the maintenance of high [EPO] levels following intermittent altitude exposure did not stimulate erythrocyte volume expansion. Future studies with more precise measures of plasma and erythrocyte volumes are needed to fully answer these questions.

When comparing the frequency and severity of signs and symptoms of AMS in our study to the results from three previous studies on individuals residing at 4,300 m for 3-wk (Table 11), we found that intermittent exposures to 4,300 m were equally as effective as chronic altitude residence in eliminating the severity and frequency of AMS. The incidence of AMS (i.e., 50%) in our study was comparable to the mean results reported in other studies at this altitude (31,59,84,85). The highest AMS-C score in our study occurred at 12-h post exposure and was comparable to the mean highest AMS-C score reported from these four chronic altitude residence studies (Table 11). Two studies have looked at the effects of intermittent altitude exposures on AMS severity and frequency. One study found no change in AMS symptoms between SL and altitude in shift workers intermittently exposed to 4,200 m compared to a group of non-acclimatized controls (17). Thus, intermittent altitude exposure eliminated symptoms of AMS in these shift workers upon subsequent exposure to altitude. Another study (18) measured AMS in lowlanders after breathing a hypoxic gas mixture that simulated

3,200-3,550 m for 8 $h \cdot d^{-1}$ for 10 d and compared their responses to a group of non-acclimatized controls. This study reported no differences in AMS symptomatology between groups upon exposure to 4,500 m. However, this study was complicated by the fact that up to five breaks of varying duration were given from breathing the hypoxic gases during the course of the 8 h day. Furthermore, although the inspired PO_2 was known, the actual degree of hypoxemia (i.e., SaO_2) was never measured in the volunteers breathing the hypoxic gas mixture. Thus, the results from this study are tenuous at best.

Many mechanisms have been proposed and extensively reviewed concerning the development of AMS (36,38). Two commonly proposed mechanisms for the development of AMS are the absence of normal altitude diuresis, evidenced by a lack of increased urine output, (37,99,111) and relative hypoventilation upon acute altitude exposure (37,69,83). We found a strong negative correlation between the presence of sickness and both decreased 24-h urine output and resting SaO_2. There was also a significant difference in these variables between the sick and non-sick volunteers 24 h after initial altitude exposure (Figure 5). These findings are consistent with the concept that diuresis and loss of body water, as well as a brisk ventilatory response, are favorable responses to acute high altitude exposure. A third mechanism suggested for the development of AMS is increased sympathetic activity upon acute altitude exposure (9). However, our similar epinephrine and norepinephrine data at rest 24 h after altitude exposure at both PreAc and PostAc do not lend support for this hypothesis. Fulco et al. (31) also reported no group differences in AMS between placebo and ß-blocked subjects after 24 h of altitude exposure. Thus, this research lends further support for the hypothesis that fluid retention and hypoventilation contribute to increased symptoms of AMS.

Improvements in submaximal but not maximal physical work performance are often reported following chronic altitude residence (116). When comparing our $\dot{V}O_{2max}$ results to results from seven previous studies conducted on individuals residing at 4,300 m for 3 wk, we found that the 22.0% mean decrease in $\dot{V}O_{2max}$ from SL to PreAc was approximately the same as in other studies where individuals were acutely exposed to 4,300 m (Table 12). However, the 18.0% increase in $\dot{V}O_{2max}$ from PreAc to PostAc in this study was dramatically different from the 0% increase reported following chronic altitude residence (Table 4). Intermittent altitude exposures appear to be a superior method for improving $\dot{V}O_{2max}$, measured at altitude, than continual residence at

altitude. It is unlikely that the observed improvements in $\dot{V}O_{2max}$ were due to a training effect given that two practice sessions were given, one at SL and one at altitude, for all physical performance tests before any data were collected. Others have also reported dramatic improvements in $\dot{V}O_{2max}$, measured at altitude, after intermittent altitude exposures involving no sleep at altitude (Table 1). In studies involving intermittent exposures to altitude during sleeping hours, none have reported *altitude* $\dot{V}O_{2max}$ measurements (4,58,73,74,100). Thus, whether intermittent exposures to altitude, involving sleep at altitude, would also improve altitude $\dot{V}O_{2max}$ remains unresolved.

Multiple reasons may contribute to this dramatic improvement in $\dot{V}O_{2max}$ following intermittent altitude exposures. First, body weight was maintained throughout this study (Table 2). Often during altitude residence studies, individuals lose a significant amount of body weight (114,117) that may include muscle mass. Thus, maintenance of muscle fiber size may have contributed to the improvement in $\dot{V}O_{2max}$. Second, PV was maintained from PreAc to PostAc. Typically, plasma volume decreases 15%-25% from baseline SL values following chronic altitude residence. Although controversial (107), the decrease in PV and maximal HR following chronic altitude acclimatization likely contributes to the decrease in cardiac output. Thus, the increase in CaO_2 with altitude acclimatization is offset by the decrease in cardiac output resulting in no change in $\dot{V}O_{2max}$ (35). With intermittent altitude exposure, the maximal cardiac stroke volume, estimated by O_2 pulse, was increased and maximal HR was maintained from PreAc to PostAc . Thus, estimated maximal cardiac output was increased from PreAc to PostAc and likely contributed to the observed increase in $\dot{V}O_{2max}$.

Third, hematological adaptations did occur, as evidenced by increased resting and maximal [Hb] measured 1-4 h following initial altitude exposure (Table 18). This increase in [Hb] in combination with the increased SaO_2 directly increased CaO_2 from PreAc to PostAc (Table 10). The improved O_2 delivery to the working muscle likely contributed to the observed increase in $\dot{V}O_{2max}$. Lastly, half of the volunteers did complete a training program. This intensity of training at SL has been shown to improve $\dot{V}O_{2max}$ in untrained volunteers anywhere from 5%-15% (42,43). Therefore, a portion of the 18.0% combined group improvement may be attributed to exercise training. When group differences were considered for $\dot{V}O_{2max}$, the PS group improved 13.0±13.1% from PreAc to PostAc, while the ET group improved 23.0±8.7%. Thus, we estimate that approximately half (i.e, ((23%-13%)/23%)) of the 23.0% improvement in $\dot{V}O_{2max}$ in the ET group was due to exercise training. However, passive sitting at altitude

was likely responsible for the remaining improvement in $\dot{V}O_{2max}$ in both groups. This interpretation is consistent with the results from another intermittent altitude study, which attributed the 10% increase in $\dot{V}O_{2max}$ from pre- to post-intermittent altitude exposures to hypoxia alone (6).

Nine other studies have examined the change in $\dot{V}O_{2max}$, measured at altitude, in untrained volunteers where exercise training has been combined with intermittent altitude exposures (Table 1). These studies have reported 5%-15% improvements in $\dot{V}O_{2max}$ from pre- to post-training programs combined with intermittent exposures to either hypobaric hypoxia or hypoxic gases. Our 23.0% increase in $\dot{V}O_{2max}$ in the ET group was higher than in these studies. Reasons for this may be related to the fact that while the mean training altitude, time, intensity, and duration from these six studies were similar to our study, the total exposure hours to altitude per day in our study (240 min) was quadruple the mean amount from these other studies. Others intermittent altitude studies have measured no change in $\dot{V}O_{2max}$ from pre- to post-training (56,63,104). The reason for the differing results may be related to the fact that these studies were done on well-trained athletes that had little room for improving $\dot{V}O_{2max}$.

Interestingly, the lactate paradox (i.e., lower maximal [La] following chronic altitude exposure compared to acute altitude exposure), which has been repeatedly observed in chronic altitude acclimatization studies (79), was not consistently observed in this study. Although resting and maximal [La] remained unchanged from PreAc to PostAc, submaximal [La] at 70% of pre-training altitude-specific $\dot{V}O_{2max}$ was lower at PostAc compared to PreAc. However, $\dot{V}O_{2max}$ was also increased from PreAc to PostAc. Thus, although the absolute workload was the same at both PreAc and PostAc, the relative workload was lower at PostAc and may have contributed to the lower [La] accumulation. Furthermore, there was no evidence for any change in substrate utilization as evidenced by the unchanged RER at rest, submaximal workloads, or maximal workloads from PreAc to PostAc. Other intermittent altitude studies have reported lower lactate accumulations at the same workload (19,56,70,86,103) following intermittent altitude exposures while others have reported no changes (22,25). Differences between studies may be due to subject populations (i.e., trained vs. untrained), training workloads employed (i.e., relative vs. absolute), changes in $\dot{V}O_{2max}$ from pre to post-intermittent exposure, nutritional control, and fluid hydration status (i.e., dehydrated, euhydrated, hyperhydrated).

Intermittent altitude exposures also resulted in great improvements in END_{wb} time at altitude. The improvement in END_{wb} time from PreAc to PostAc cannot be attributed to differences in diet or fluid hydration status as these were controlled before each trial. When comparing our results to the results of two chronic altitude residence studies (44,60), we found our ~21% improvement in submaximal endurance performance time lower than the ~45% and 60% improvement reported by Maher et al. (60) and Horstman et al. (44), respectively. However, in both of those studies, the submaximal endurance performance test was to exhaustion and thus open-ended. Our submaximal endurance performance test was closed-ended and thus the room for improvement was much less. Another study employing intermittent altitude exposures that involved no sleeping at altitude (104) measured submaximal exercise time to exhaustion and reported a 34% improvement. In studies involving intermittent exposures to altitude during sleeping hours, submaximal exercise performance has improved following intermittent altitude exposures in some (58,73) but not all (74) studies. We did expect differences in END_{wb} time between groups given the exercise training employed in our protocol but we did not find them. However, the ET group improved their END_{wb} time 25.1±8.3% from PreAc to PostAc while the PS group improved 16.1±22.6 % and small subject numbers may have obscured potentially significant group differences. Again, it appears that approximately 36% (i.e, 25%-16%/25%) of the improvement in END_{wb} time was due to exercise training while passive sitting accounted for the remaining 64% of the improvement in END_{wb}.

During the fixed-work submaximal test (i.e., complete a given amount of work), the volunteers were able to maintain a 24.2% higher absolute VO_2 at PostAc compared to PreAc (Figure 8). Therefore, they were able to complete the absolute amount of work in a shorter time at PostAc compared to PreAc. The percentage of improvement in the VO_2 maintained (24.2%) was very similar to their percent improvement in END_{wb} time (21.4%). However, the volunteers did not improve the percentage of altitude-specific VO_{2max} maintained during the fixed-work submaximal test from PreAc to PostAc (Figure 9). Thus, the improvement in END_{wb} appears to be directly related to the improvement in VO_{2max} from PreAc to PostAc ($r=0.99$; $P=0.0001$).

Others have attributed the improvement in submaximal exercise performance, despite unchanged VO_{2max}, to both increased fat oxidation and subsequent sparing of muscle glycogen, as well as less circulatory strain following chronic altitude residence. Following our intermittent altitude exposures, neither of these reasons appears to

contribute to the improvement in END_{wb} time. Neither the hormones (i.e., [EPI], [NOR], and [COR]) affecting metabolism were changed from PreAc to PostAc, nor was RER, measured at any time point, affected by the 15-d of intermittent altitude exposure. We did not find less [La] at exhaustion during the END_{wb} test, but our subjects performed the total amount of work in less time at PostAc. Lessening of cardiac strain does not appear to be a reason for the improved END_{wb} time at PostAc compared to PreAc. Both HR and O_2 pulse at any time point during the END_{wb} test were unchanged from PreAc to PostAc. The CaO_2 was higher PostAc compared to PreAc, primarily due to the effects of ventilatory acclimatization, and thus may have contributed to the increase in END_{wb}. However, others have found that a decrease in blood flow offsets the higher CaO_2 following chronic altitude acclimatization; and O_2 delivery remains the same (12,113). Whether a decrease in blood flow occurred in our study remains unknown. However, even if blood flow did decrease, the potential enhancement of equilibration time in the muscle capillary could also potentially improve endurance exercise performance.

Studies using one-legged exercise training during intermittent exposures to hypobaric hypoxia, hypoxic gases or ischemia have all reported dramatic improvements in both maximal and submaximal exercise performance following a period of intermittent altitude exposures (Table 30). Most of these improvements were attributed to biochemical and structural changes within the muscle such as increased citrate synthase, mitochondrial density, and myoglobin. However, all of these studies were complicated by the fact that the leg trained in hypoxia was trained at higher relative exercise intensity than the leg trained in normoxia. A greater local tissue hypoxia and stimulus for change may have occurred in the hypoxic-trained leg (81). However, in our study, both legs were trained at the same relative exercise intensity in each environmental condition and muscle biopsies were not taken. Therefore, we cannot determine whether or not muscle biochemical and structural changes contributed to our observed improvements in END_{wb} following 15 d of intermittent altitude exposure.

Table 30. Results of Maximal Oxygen Uptake (VO_{2max}) and Submaximal One-Legged Endurance Performance from Three Studies on Untrained Volunteers Before and After a Period of Combined Exercise Training and Intermittent Exposures to Either Hypobaric Hypoxia, Hypoxic Gases, or Ischemia Simulating Altitude.

Study	Altitude (m)	Training Intensity (% altitude VO_{2max})	Days	Days $\cdot wk^{-1}$	Minutes $\cdot Day^{-1}$	Pre-training VO_{2max} ($l \cdot min^{-1}$)	Post-training VO_{2max} ($l \cdot min^{-1}$)	% Change in VO_{2max}	% Change in Endur-ance Time
(64)†	~3,000	~75	56	3	30			11.0	510
(102)†	2,300	65	28	4	30				313
(48)	n/a	n/a	28	4	45			25.0	
Mean (single-leg)	**2,650**	**~70**	**37**	**4**	**35**			**18.0**	**412**

Not only was END_{wb} time improved following intermittent altitude exposures, END_{sm} time was also dramatically improved (Figure 10). Three other studies have examined improvements in small muscle (i.e., adductor pollicis) endurance performance following chronic altitude acclimatization (Table 29). Two of these studies were done on men (27,28) and the other was done on women (30). Our 64.5% improvement in END_{sm} from PreAc to PostAc was almost double the mean amount reported in these other studies. Reason for the large difference between studies may have to do with the timing of our measurement. In all of the chronic altitude acclimatization studies, the acute altitude exposure was 24-48 h following initial introduction to altitude. However, in our intermittent study, the acute altitude exposure was 1-4 h following initial introduction to altitude. Typically, small muscle function shows the most deterioration within the first few hours of altitude exposure (C. Fulco, personal communication, October, 2001). A larger initial decrement in small muscle endurance performance upon acute altitude exposure from SL values leaves greater room for improvement following altitude acclimatization. In fact, when the data were standardized for the differences in these initial decrements, we regained 138% of the initial loss in END_{sm} from PreAc to PostAc while the mean regain in small muscle endurance performance in the other chronic altitude studies was 118%. Therefore, intermittent exposure to altitude appears to accomplish the same or greater amount of

acclimatization for small muscle endurance performance as chronic altitude acclimatization.

Reasons for the large improvements in END_{sm} following intermittent altitude exposures may be related to an augmented blood-to-tissue PO_2 gradient, as our arterial PO_2 was higher following intermittent altitude exposures (Table 20). Although others have measured no change in O_2 delivery during one-legged exercise from acute to chronic altitude exposures (12,113), physical performance measures were not made. The decrease in blood flow that typically offsets the increase in CaO_2 following chronic altitude acclimatization results in a longer equilibration time in the muscle capillary that may eventually enhance endurance performance. The lower [La] accumulation during whole body submaximal exercise may also have occurred during small muscle submaximal exercise and contributed to the performance improvements. Whether or not muscle buffering capacity was improved following intermittent altitude exposures, which has been reported following chronic altitude residence (66,90), cannot be determined from our data. However, blood buffering capacity was not changed as evidenced by the similar decrement in $[HCO_3^-]$ following intermittent altitude exposure as after chronic altitude residence. As in the chronic altitude residence studies (27,28,30), we found no differences in the MVC of the adductor pollicis at SL, PreAc, or PostAc.

Limited data were collected on training days during the 15-d intermittent acclimatization program. Although resting SaO_2 was increased from the first day of training to the last day of training (Figure 11), the pattern of increase was not necessarily linear. Both training HR and MAP did not change from the 1st to 15th day of training. Although we had hoped to determine whether we could shorten the number of days needed to acclimatize to 4,300 m, the lack of a statistically significant change in SaO_2, a major determinant of altitude acclimatization, until the 15th day of training suggests otherwise. However, there was a large variance in individual SaO_2 values during the training days. Upon closer examination of Figure 11, it appears that the majority of the increase in SaO_2 occurs by day 9 and then levels off until day 15. Thus, the low subject numbers and large variances may have obscured potentially significant differences earlier in the acclimatization protocol. Thus, it appears that 9 d may be all that is needed to achieve optimal acclimatization effects.

CONCLUSIONS

In conclusion, we found that 3 wk of intermittent (i.e., $4h \cdot d^{-1}$; $5d \cdot wk^{-1}$) exposures to 4,300 m accomplished 50%-100% of the expected adaptation to altitude, based on improvements in submaximal endurance performance and absence of altitude illness, when compared to previous studies where individuals resided at 4,300 m for 3 wk. Exercise training during intermittent exposures to 4,300 m altitude did not have a greater effect on acclimatizing an individual to 4,300 m altitude than passively sitting at 4,300 m altitude. Ventilatory acclimatization was accomplished to a larger degree than hematological acclimatization. However, the repeated triggering effect of [EPO] with intermittent altitude exposures may have a greater potential to increase blood volume than continual exposure to altitude. Acute mountain sickness was eliminated by intermittent altitude exposures. Intermittent altitude exposures resulted in greater improvements in VO_{2max} and small-muscle endurance performance than continual altitude residence and similar improvements in whole-body endurance performance. At least 9 d of intermittent altitude exposures may be needed to achieve optimal acclimatization effects.

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